The Russell Sage Institute of Pathology

IN AFFILIATION WITH

The Second Medical Division of Bellevue Hospital

CLINICAL CALORIMETRY

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The Russell Sage Institute of Pathology

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NEW YORK

CLINICAL CALORIMETRY

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CHICAGO
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1916

CLINICAL CALORIMETRY

FIRST PAPER

A RESPIRATION CALORIMETER FOR THE STUDY OF DISEASE *

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NEW YORK

HISTORICAL

A respiration calorimeter is an apparatus designed for the measurement of the gaseous exchange between a living organism and the atmosphere which surrounds it, and the simultaneous measurement of the quantity of heat produced by that organism.

The first contrivance of this nature was described by Lavoisier in 1780. It will be remembered that Lavoisier was the first to comprehend the significance of the then newly discovered oxygen. Primitive though the apparatus, yet intellectually inspiring was the mind which so early grasped the principles and understood many of the difficulties.

Apparatus for the measurement of the respiratory exchange was perfected before that for the measurement of heat production. Thus, Regnault and Rieset[1] in 1850 designed an air-tight apparatus in which an animal was placed; the carbonic acid formed in it was removed by pumping the air into flasks filled with potash, and oxygen was added from time to time as it was required. This is the *closed circuit* system which in a modified form is used to-day.

The historic respiration apparatus of Pettenkofer[2] and Voit was completed in 1862. This machine was capable of measuring the carbon dioxid output of a man within 1 per cent. of error. As early as 1866 Voit began computing from the substances oxidized in the body the quantity of heat which should have arisen from the destruction of those substances. This method is known as *indirect calorimetry*.

In 1885, Rubner, working in Voit's laboratory, published results concerning the calorimetry of foods. Accurate determinations of the

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* From the Russell Sage Institute of Pathology, in affiliation with the Second Medical Division of Bellevue Hospital.

1. Regnault and Rieset: Ann. d. Chem. u. Pharmakol., 1850, lxxiii, 92, 129, 257.

2. Pettenkofer: Ann. d. Chem. u. Pharmakol. Supplement 2, 1862.

heat value of urea, and of dry urinary solids were made for the first time. This work established biological standards for the heat values of proteins, carbohydrates and fats which are to-day accepted.

About the same time a calorimeter for the measurement of the heat production in man was set up in Voit's laboratory and many experiments were made with it by Carl Voit and his brother Erwin Voit. The results were apparently not satisfactory, for nothing was ever published on the subject. At this time Atwater was in Voit's laboratory, and in 1888 published from that laboratory an article on the absorption of the flesh of fish.

Atwater's interest in nutrition had already been stimulated by Johnson and Brewer at Yale, and through studies in agricultural and physiological chemistry in Berlin in 1869-71. In 1877 he began investigations into dietary requirements of the people. It was Atwater's association with Voit and with Rubner, however, which gave him his knowledge of the principles of the subject of calorimetry as applied to the living organism. These facts, which are not widely known, emphasize again the overwhelming debt which American science owes to Germany.

In 1894 Rubner built the first successful respiration calorimeter. He built it largely with his own hands and with the very moderate means available in his laboratory at Marburg where he had become professor of hygiene. Voit, on hearing the news, said that it was the most important invention of its kind since the invention of the thermometer. Rubner's calorimeter, which measured the heat production of a dog, was associated with the mechanism of a Pettenkofer respiration apparatus which determined the carbonic acid output of the animal. Thus *indirect calorimetry* could be compared with *direct calorimetry*. For example, if the nitrogen in the urine and feces of a dog fed with meat and fat were determined, and this nitrogen were multiplied by 6.25, the quantity of protein destroyed could be estimated. Since each gram of protein yields 4.1 calories of heat in the body, the quantity of heat produced from protein would be

$$\text{Grams excreted N} \times 6.25 \times 4.1$$

To estimate the quantity of fat oxidized the quantity of carbon contained in the protein destroyed (which amounts to grams excreted N $\times$ 3.28) was deducted from the quantity of carbon contained in the

3. For the history of animal calorimetry see Rubner: Tigerstedt's Handbuch der physiol. Methodik. i, 150; Johansson, Abderhalden's Handbuch der biochem. Arbeitsmethoden, Berlin, 1910, iii, 1114.

excreta, that is, the sum of that in the urine, feces and respiration. The remainder represented the quantity of expired carbon derived from the oxidation of fat. Since fat contains 76.5 per cent. of carbon and 1 gm. of fat yields 9.3 calories, it was easy to calculate the heat production derived from fat. Recapitulating, one may express the heat produced from fat in the formula:

$$\text{Total C} - (\text{N} \times 3.28) \text{ divided by } 76.5 \times 100 \times 9.3$$

Adding together the heat calculated as that which should have arisen from the protein and fat metabolized, Rubner found that this sum was exactly the amount of heat given off by the animal as measured by the calorimeter. This was the first long-sought demonstration of the law of the conservation of energy applied to animal life.

After returning to America, Atwater in 1892 began work on a calorimeter which could measure the heat production in man. In 1894 the United States government began to appropriate funds for investigations into the nutrition of the people and placed the distribution of these funds in the hands of Professor Atwater. A portion was wisely used in the construction of the Atwater-Rosa[4] respiration calorimeter, the earlier description of which appeared in 1897. In 1893 C. F. Langworthy and in 1895 F. G. Benedict became associated with the undertaking. Shortly after the completion of the apparatus, Rosa, the expert physicist, to whose skill its successful completion was largely indebted, retired from direct association with the enterprise, although, as professor of physics at Wesleyan he was still frequently consulted until, in 1901, he became chief physicist of the Bureau of Standards at Washington. The Atwater-Rosa calorimeter demonstrated that direct and indirect calorimetry agreed in man, not only during rest, but also during periods when mechanical work was performed.

The original Atwater-Rosa calorimeter was associated with a respiration apparatus of the type designed by Pettenkofer, which measured only the carbon dioxid output. Calculated on this basis the production of heat might show a maximum error of 24 per cent., depending on whether carbohydrate or fat was being oxidized. At a later date funds were granted to Atwater by the Carnegie Institution in order to apply the principle of the closed circuit of Regnault and Rieset to the apparatus so that the oxygen absorption might also be determined. The modification of the apparatus along these lines was begun in 1902, and the work accomplished during 1903 to 1905 was done during a period when Atwater was in full control of the undertaking. Atwater's illness

4. Atwater and Rosa: Report of the Storrs Agric. Exper. Station, 1897, p. 212.

began in 1905, his retirement took place in 1906 and he died in 1907.

With the improved apparatus, publication[5] concerning which fell in 1905, not only heat production and carbon dioxid output were accurately measured, but the absorption of oxygen as well. It thus became possible to measure not only the non-protein carbon in the respiration, but also to calculate how much of the oxygen absorbed was devoted to the destruction of non-protein material; that is to say, fat and carbohydrate. The value of this knowledge becomes apparent when it is realized that one liter of oxygen used for the oxidation of fat yields 4.686 calories, whereas when the same volume is used to oxidize starch 5.047 calories are set free, a difference of over 7 per cent. When carbohydrate is oxidized the volume of oxygen absorbed is equal to the volume of carbon dioxid expired and the *respiratory quotient* equals unity.

$$\text{R. Q. equals } \frac{\text{Vol. } CO_2}{\text{Vol. } O_2} = 1$$

When fat is oxidized, however, the respiratory quotient is only 0.70. Respiratory quotients (corrected from protein influence) which run intermediate between 0.70 and 1.00 are deemed to represent the oxidation of mixtures of carbohydrates and fats, and the heat value of a liter of oxygen varies accordingly. Thus a quotient of 0.85 represents the oxidation of fat and carbohydrate together in such a proportion that 49 per cent. of the calories produced are derived from carbohydrate and 51 per cent. from fat. Under these circumstances, 1 liter of absorbed oxygen represents 4.863 calories liberated in the organism. Tables giving these data were first published by Zuntz.[6]

The ability to determine the oxygen absorption with exactness abolished a possible error of considerable magnitude in the calculations of indirect calorimetry. This improvement brought the apparatus to a high degree of perfection. The Carnegie Institution of Washington has richly provided for the higher development of the work in the Nutrition Laboratory at Boston, which represents the realization of Atwater's ambition for the establishment of a separate laboratory for this work. Dr. Benedict is here the controlling genius, while the original Wesleyan calorimeter, now removed to Washington, is under the direction of Dr. C. F. Langworthy.

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5. Atwater and Benedict: Carnegie Institution of Washington, 1905, Pub. 42. See also, Benedict and Carpenter: 1910, Pub. 123.

6. Zuntz and Schumburg: Studien zu einer Physiologie des Marches, Berlin, 1901. See also, Williams, Riche and Lusk (Jour. Biol. Chem., 1912, xii, 357), for other references.

ANIMAL CALORIMETRY AT THE CORNELL UNIVERSITY MEDICAL COLLEGE

At the time of my appointment to the professorship of physiology at the Cornell University Medical College, the authorities liberally provided for the construction of a respiration apparatus. Dr. Murlin spent a part of the summer with Dr. Benedict in Boston, where he freely received every privilege of the laboratory. After considerable discussion, I decided to have a calorimeter constructed which was small enough for use with dogs and babies, work which, up to that time, had not been included in the program of the Boston laboratory. The construction of this apparatus was entrusted to the capable management of Dr. H. B. Williams.[7] Full and grateful acknowledgment is due to Dr. F. G. Benedict, who has ever given all that counsel which his unique experience in calorimeter construction makes of highest value.

The problem of the measurement of 7 calories of heat produced in an hour by a baby weighing 3 kg. was different from that presented by the measurement of 70 calories produced by an adult. This led to the addition to the calorimeter of certain refinements in technical construction which are due to Dr. Williams. The small calorimeter has been successfully used in many experiments on dogs and babies. For the first time direct and indirect calorimetry were found to agree during hourly periods of experimentation.

The method employed with dogs was to determine the *basal metabolism* as measured by that quantity of heat which was produced by the resting animal when there was no food in the gastro-intestinal tract, and to compare this metabolism with that found at times following the ingestion of various foods. It was found that three or four hours of observation sufficed to indicate the influence of ingested food.

The satisfactory working of the apparatus used in accordance with these principles encouraged me to believe that valuable results might be obtained concerning the nutrition of patients if a similar, though larger, apparatus were placed in Bellevue Hospital. Before embarking on the undertaking, inquiry was made of Dr. Benedict if he did not desire to investigate this field by establishing a calorimeter in the Peter Bent Brigham Hospital in Boston. As the reply was in the negative, it appeared justifiable to seek money and opportunity for the accomplishment of this work.

Sufficient funds were obtained from the Russell Sage Institute of Pathology for a period of five years. The former arrangement between this institute and the City Hospital had just been terminated. A new arrangement was entered into with the trustees of Bellevue Hospital

7. Williams: Jour. Biol. Chem., 1912, xii, 317.

which enabled the institute to construct the first respiration calorimeter ever established in a hospital. Dr. Eugene F. Du Bois was appointed medical director, and the whole undertaking has enjoyed the faithful service of chemists, mechanics and nurses who have contributed to its success. A factor of especial encouragement has been the personal interest in the undertaking manifested by the visiting physicians, Drs. W. Gilman Thompson, C. L. Dana and Warren Coleman. The last-named has taken part in the actual work of the institute.

It is also a pleasure to acknowledge with thanks many helpful suggestions made by Drs. Langworthy and Milner of Washington.

Fig. 1.—Respiration calorimeter with the patient half-way in. On his chest can be seen the tube of the Bowles stethoscope strapped over the heart. Coiled up on the wall is the rectal thermometer not yet inserted. Just below this is one of the units of the air thermometer and to the right is the telephone.

An Atwater-Rosa-Benedict respiration calorimeter, together with the instruments of precision applied to it by Williams, and certain new modifications which were the result of advice and experience, was established in Bellevue Hospital. The papers which follow are descriptive of the calorimeter (Fig. 1) and the results obtained with it. The patient lies quietly for three or four hours on a comfortable bed in the chamber of the apparatus, breathing the purest air, without the possi-

bility of harm. The long periods of the older respiration chambers and the nose- or mouth-pieces of the short-period apparatus are not disturbing factors. For the benefit of those who are interested in the work and who do not care to follow the details of the technical description of the apparatus, the following summary will suffice.

PRINCIPLE OF THE ATWATER-ROSA-BENEDICT RESPIRATION CALORIMETER

The apparatus is divided into two functional parts, one for measuring the gaseous exchange, the other for measuring the heat production of the subject. A schematic presentation is here given (Fig. 2).

The Gas Analysis.—The inner lining of the apparatus presents an air tight copper box having a capacity of 1,123 liters. One end of the box, through which the patient lying on the bed is admitted, may be closed with a glass plate by means of wax. The air within the box is purified by drawing it out of an opening in the box through a rubber tube and forcing it by means of a rotary blower through a system of *absorbers,* whence it returns again to the box by another rubber tube. It passes (see diagram) first through sulphuric acid (1), which removes the water, then through moist soda lime (2), which removes the carbon dioxid, and next through sulphuric acid (3), which absorbs the moisture taken from the soda lime. If the bottles be previously weighed, the gain in weight of 1 represents water absorbed, and the gain in weight of 2 plus 3 equals the carbon dioxid absorbed. By this method the water and carbon dioxid produced by a man are taken from the air, while oxygen within the chamber is being absorbed by the man himself. This causes a diminution in the volume of the contents of the box. In order to replace the oxygen used, oxygen is automatically fed into the system from an oxygen cylinder which may be weighed before and after the period. The automatic feeding of oxygen into the box is accomplished by means of a spirometer whose interior is connected with the interior of the calorimeter chamber. As the volume of the air in the box decreases, the spirometer falls until a certain point is reached, at which an electric contact releases a clamp, which allows oxygen from the oxygen cylinder to enter the box, causing the spirometer to rise, break its electric contact and clamp off the oxygen supply. So sensitive is the spirometer to the movement of the patient that a device called a "work adder" has been attached to it, which records the subject's movements.

At the beginning of an hourly period of experimentation an observer at the table calls "time." At this instant the rotary blower is stopped, the air current switched so as to pass through a new set of weighed absorbers and then the rotary blower is started again. At the word "time" an operator also turns a pet-cock which cuts off the respiratory chamber from the spirometer cylinder, which is then filled, always to a given point, with oxygen from the oxygen cylinder. The pet-cock is now opened and a freshly weighed oxygen cylinder is placed in the position of the other, which is removed. Repeating these procedures an hour later, one may determine by difference in weight the gain of water and carbon dioxid by the absorbers and the loss of oxygen by the cylinder. The figures are subject to corrections due to (1) gain or loss of water or carbon dioxid content in the box itself, during the period, which gain or loss must be added to or subtracted from the increase in weight of the absorber system. This gain or loss of water and carbon dioxid in the box also affects the volume of the air in the box and, therefore, the quantity of oxygen admitted, as do, in addition (2), a change in temperature within the box and (3) a change in barometric pressure. These corrections must be made in order to determine whether oxygen is to be added or subtracted from the quantity which has been furnished from the oxygen cylinder. The result

gives the quantity of oxygen which the man has absorbed. It is apparent that all the errors of determination fall on the oxygen, and yet the exactness of the method is witnessed by the close approximation in alcohol check experiments of the theoretical and actual values for oxygen consumed.

If a person in the calorimeter moves even the arm during the critical moments just before "time" is called, the increased local heating of the air may cause the spirometer to rise to a considerable height, of which the air

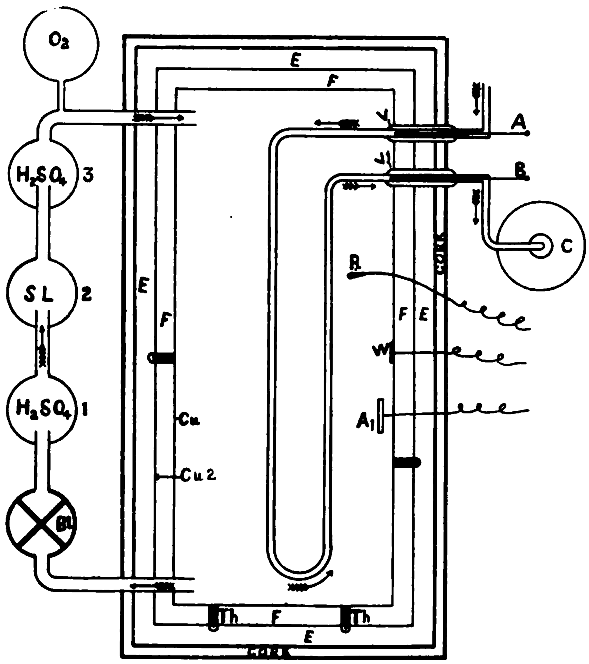

Fig. 2.—Schematic diagram of the Atwater-Rosa-Benedict respiration calorimeter.

Ventilating System:
- O_2, Oxygen introduced as consumed by subject.
- 3, H_2SO_4 to catch moisture given off by soda lime.
- 2. Soda lime to remove CO_2.
- 1, H_2SO_4 to remove moisture given off by patient.
- Bl., Blower to keep air in circulation.

Indirect Calorimetry:
- Increase in weight of H_2SO_4 (1) = water elimination of subject.
- Increase in weight of soda lime (2) + increase in weight of H_2SO_4 (3) = CO_2 elimination.
- Decrease in weight of oxygen tank = oxygen consumption of subject.

Heat-Absorbing System:
- A, Thermometer to record temperature of ingoing water.
- B, Thermometer to record temperature of outgoing water.
- V, Vacuum jacket.
- C, Tank for weighing water which has passed through calorimeter each hour.
- W, Thermometer for measuring temperature of wall.
- A1, Thermometer for measuring temperature of the air.
- R, Rectal thermometer for measuring temperature of subject.

Direct Calorimetry:
- Average difference of A and B × liters of water + (gm. water eliminated × 0.586) ± (change in temperature of wall × hydrothermal equivalent of box) ± (change of temperature of body × hydrothermal equivalent of body) = total calories produced.

Th, thermocouple; *Cu*, inner copper wall; *Cu₂*, outer copper wall; *E*, *F*, dead air spaces.

thermometers inside the box fail to make compensatory record, and the oxygen determination will be too low in that hour and too high in the next.

Analysis of the air in the interior of the chamber is made just before the beginning of each hour by passing ten liters of air from the box through three U-tubes containing, respectively, sulphuric acid, soda lime and sulphuric acid, then through a Bohr gas meter and back into the box again. This is called the "residual analysis."

Under the conditions present in the respiration apparatus, carbon dioxid is measured with the greatest ease and accuracy. Oxygen is also measured with accuracy if the person within the box lies perfectly quietly for ten minutes before the end of the period, whereas water production is the least accurate of all the determinations, on account of the varying hygroscopic condition of the walls, bedding and other surfaces within the closed spaces of the apparatus.

The Measurement of Heat Produced. — Roughly speaking, one-quarter of the heat eliminated by a man is present in the water vapor which is absorbed by the first sulphuric acid bottle on the absorber table. At 20 degrees C. 0.586 calories are contained as latent heat in 1 gm. of vaporized water.

The rest of the heat loss takes place by radiation and conduction. It is this heat which is measured by the calorimeter, itself. The mechanism of the calorimeter is essentially two-fold. In the first place, there is no heat loss through the walls of the apparatus, and, secondly, the heat produced by a man within is removed from the chamber by a current of cold water flowing through copper tubes suspended from the upper wall of the chamber. If the walls allowed no heat to pass, it is obvious that without the cooling effect of the water-pipes the temperature of the air in the box would soon attain the temperature of the human body instead of being about 23 C., at which it is usually held. The apparatus is therefore a constant-temperature, water-cooled calorimeter. It is evident that if no heat is allowed to pass through the walls of the calorimeter, then the heat produced within the chamber will be removed in the current of cold water flowing through the heat-absorbing pipes inside the chamber of the apparatus. If the temperatures of the ingoing and of the outgoing water are known and the quantity of water which has passed through the heat-absorber during an hour is measured, the quantity of heat carried away in the current of water can be accurately determined. For example, if the difference between the temperature of the ingoing and outgoing water is 2.50 degrees, and 20 liters of water have passed through the heat absorber in one hour, then 50 calories of heat have been carried away from the apparatus during the period. If the temperature of the walls within the apparatus has undergone a change this value is subject to corrections, but otherwise the total heat elimination of the person is meas-

ured by the 50 calories so determined plus the heat value of water vaporized during the hour.

To obtain an even flow of water through the heat-absorber the water is supplied from a constant-level tank placed above the calorimeter. To obtain ingoing water of an even temperature, Williams passed the previously ice-cooled water current through a Gouy temperature regulator and then through a current regulator designed by himself. These improvements allow the ingoing water to enter the calorimeter at a temperature which may not vary more than 0.02 C. during hours of experimentation and, for the first time, permitted the exact measurement of small quantities of heat in this type of apparatus. The temperatures of the ingoing and outgoing water are taken every four minutes by electrical resistance thermometers and are read in connection with a galvanometer and Kohlrausch bridge on an observer's table. The quantity of the water-flow is determined by weighing; the water is diverted at the call of "time," so that the exact quantity for the hour is collected in a previously weighed receptacle.

Having learned how the heat produced within the apparatus is carried away, the problem of how to prevent loss of heat through the walls of the chamber remains to be discussed. This was accomplished through a device introduced by Rosa. The calorimeter is constructed of three walls, an inner copper wall which has already been described as the lining of the respiration chamber, an outer copper wall separated from the inner wall by a space of dead air, and an insulating wall (made of two layers of "compo-board," the space between them being filled with cork), which insulating wall is separated from the outer copper wall by a second space containing dead air. It is obvious that if the inner and outer copper walls of the calorimeter have the same temperature there will be no exchange of heat between them. Therefore, to prevent a gain or loss of heat by the inner wall, it is necessary to maintain the outer wall always at exactly the same temperature as the inner wall, under which circumstances the latter cannot gain or lose heat to its neighbor.

In order to detect differences in temperature between the outer and inner walls Rosa arranged thermo-couples in series between the two walls. In this fashion the top, sides and bottom of the box are successively tested every four minutes by an operator at the observer's table to determine whether there is any difference in temperature between the outer and inner walls. If the outer wall is found to have a different temperature from the inner wall, its temperature is brought to that of the inner wall by the following device. A cooling current of water runs through pipes between the insulating and outer copper wall, and in this same space, along the line of the pipes, run "Therlo" resistance

wires carrying an electric current for the warming of this interspace (Fig. 1). By varying the intensity of the electric currents which severally supply the spaces to top, sides and bottom, the temperature of these spaces can be so controlled as to heat or cool the outer copper wall and maintain it at exactly the same temperature as the inner copper wall. This is the effective system which prevents a loss or gain of heat through the wall of the calorimeter.

Resistance thermometers are attached to the inner walls of the calorimeter, and if the temperature of the walls rises or falls between the beginning and end of the experiment, a correction must be made. It has been found that 19 calories are absorbed by the Sage calorimeter when the inner wall rises 1 degree. Conversely, 19 calories are given up by a fall of 1 degree. This is the *hydrothermal equivalent* of the box.

SCHEME OF EMPLOYMENT OF OBSERVERS IN A CALORIMETER EXPERIMENT

Period of Observation	Observer 1, at Electrical Control Table	Observer 2, in Charge of Experiment	Observer 3, Calculator
Eight minutes before	Brings wall into exact thermal equilibrium	Signals subject to lie absolutely quiet.	Starts passing first 10 L. sample of residual air through U tubes.
Five minutes before	....	Starts kymograph record of movements of spirometer	....
Four minutes before	....	....	Finishes first and starts second residual
One-half minute before	Takes final reading of air, wall and rectal temperature	Sets barometer	Finishes second residual
At "Time"	Presses button which diverts stream of water from weighing tank	Shuts spirometer off from box. Fills to standard level from oxygen tank.	Stops ventilating current of air. Turns valve to pass air through newly weighed absorbers. Starts ventilating current.
Immediately after "Time"	Starts taking readings every four minutes of ingoing and outgoing water, of air, walls, rectal and surface thermometers. Reads and adjusts temperature of top, sides and bottom of calorimeter, of the ingoing air and water every four minutes, or oftener if necessary.	Records and sets workadder. Signals to subject that he may move. Weighs oxygen tank and connects with box again. Weighs sulphuric and soda lime bottles. Connects them up again and tests for leaks. During remainder of hour counts pulse, inspects valves for leaks, adjusts temperature of room, watches subject, etc.	Weighs water tank which has received all the water from the heat absorber during the past hour. Diverts stream of water to this tank again. Records barometer. Weighs residual. Calculates results of the hour just finished.

The temperature of the air entering the box from the absorbing table is always heated to exactly the same temperature as the air leaving the box.

Finally, an electric resistance thermometer inserted 10 or 12 cm. into the rectum of the person in the calorimeter gives information regarding the retention or loss of heat in his organism. The specific heat of a man is assumed to be 0.83, that is to say, 0.83 calory raises 1 kilogram 1 degree. If, therefore, the body temperature of a man weighing 70 kg. rises or falls 1 degree, the quantity of heat lost or

gained by the body will be 70×0.83 or 58.1 calories. This is on the assumption that the rise of body temperature is everywhere the same as takes place in the rectum, a supposition which, unfortunately, is not always true.

The accompanying scheme (Table 1) gives the details regarding the employment of the three individuals who conduct a calorimeter experiment.

It may be added that special care has been taken to make the appearance of the calorimeter attractive to the eye, and that the spirit of the small ward in connection with the calorimeter work has been such that the patients have considered themselves especially fortunate when chosen for the diversion offered by a morning's occupancy of the apparatus.

CONCLUSION

The story of the Atwater-Rosa-Benedict calorimeter has been told here for the first time in brief, comprehensive, perhaps one might say semipopular language. The Williams calorimeter has shown the influence of many simple foodstuffs which were given to dogs in health and in induced disease. The Sage calorimeter reports "of the disturbances that Nature works and of her cures," without having, as concerns the sick human being, at any time, in the slightest degree, affected any patient to his disadvantage, but rather having yielded information regarding his condition which has been beneficial in his subsequent treatment.

It seems appropriate to recall the words with which Pettenkofer and Voit closed their communication regarding diabetes in the year 1867:

> Even as anatomy has been separated from physiology, so from pathological anatomy pathological physiology will arise. Only thus will we be able to obtain a more exact knowledge of the character of disease than we now possess. Able pathologists have constantly sought to open up this field. It will gratify us if this work of ours which for the first time presents a complete picture of metabolism in disease shall inspire others to devote their abilities in this direction.

CLINICAL CALORIMETRY

SECOND PAPER

THE RESPIRATION CALORIMETER OF THE RUSSELL SAGE INSTITUTE OF PATHOLOGY IN BELLEVUE HOSPITAL *

J. A. RICHE AND G. F. SODERSTROM
NEW YORK

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8. Telephone, fan and bed.
9. Electric and alcohol control experiments.
10. Limits of error in measuring heat, carbon dioxid and oxygen.
11. Determination of water elimination.
12. Adaptability of calorimeter to varying conditions.
13. Summary and conclusions.

During the short time in which the Sage calorimeter has been in operation there have been several requests for the technical details of the construction of the apparatus. It has therefore seemed advisable to publish a brief article for those interested in calorimeters. A complete description of the Atwater-Rosa-Benedict type of apparatus will be found in the monograph by Benedict and Carpenter.[1] A number of valuable improvements are added in the shorter article by Williams.[2] The earlier publications of Atwater and Rosa[3] and Atwater and Benedict[4] describe an apparatus fundamentally the same as that now employed, but for a complete understanding of the modern calorimeter it is necessary to consult the works of Benedict and Carpenter and

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* From the Russell Sage Institute of Pathology, in affiliation with the Second Medical Division of Bellevue Hospital.

1. Benedict and Carpenter: Respiration Calorimeters for Studying the Respiratory Exchange and Energy Transformations of Man, Carnegie Institution of Washington, 1910, Pub. 123.

2. Williams, H. B.: Animal Calorimetry, First Paper, A Small Respiration Calorimeter, Jour. Biol. Chem., 1912, xii, 317.

3. Atwater and Rosa: Description of a New Respiration Calorimeter, U. S. Dept. Agriculture, 1899, Bull. 63.

4. Atwater and Benedict: A Respiration Calorimeter with Appliances for the Direct Determination of Oxygen, Carnegie Institution of Washington, 1905, Pub. 42.

Williams. The description by Langworthy and Milner[5] of their ingenious automatic calorimeter should also be consulted.

The Sage calorimeter resembles Benedict's bed calorimeter, but differs in a few details. On the recommendation of Dr. Langworthy and Mr. Milner of the Department of Agriculture the outside insulation was made of pressed cork and "Compo Board." The electrical resistance thermometers for the ingoing and outgoing water were also adopted on their advice. The gas wash bottles, water heating resistance and current regulator, water coil and several other improvements were copies of those used by Williams. The soda-lime bottles and spirometer resembled those described by Benedict[6] in connection with his small apparatus.

THE CALORIMETER ROOM

The small metabolism ward to be described is situated at the southwest corner of the new medical pavilion of Bellevue Hospital. To the north of this is a hall, now converted into a diet kitchen, which leads into the calorimeter room, formerly a small ward for convalescents. The room itself (Fig. 3) is about 5 meters square and 5 meters high. On the west side, opening on a covered balcony, is a large window in front of which stand a thermostat-controlled radiator and a "Simplex" electric heater. These are enclosed in a window box in such a manner, that by means of a blower, fresh air can be drawn in through the window, driven over the heaters and out into the room. Unfortunately, the daylight is not strong and needs to be supplemented by two powerful tungsten lamps.

In the center of the room stands the calorimeter, at the side of which is the observer's platform, raised a short distance above the floor to permit the passage of the numerous water pipes and electrical conduits. On the east side of the room is the panel box where the heavy feed wires are led up from the basement. Next to this panel box are the storage batteries with charging board used in electric checks. On the south side of the room, where the door is situated, enough space has been left to wheel a stretcher with a patient to the front of the calorimeter. By making careful use of every inch a great deal of apparatus has been placed in a small room without crowding those who work there.

THE FRAME

As the photographs show, the calorimeter was made high enough at the head to allow the subject to sit upright. This increases the

5. Langworthy and Milner: Year Book U. S. Dept. Agriculture, 1910, p. 307; ibid., 1911, p. 491.
6. Benedict, F. G.: Ein Universalrespirationsapparat, Deutsch. Arch. f. klin. Med., 1912, cvii, 156.

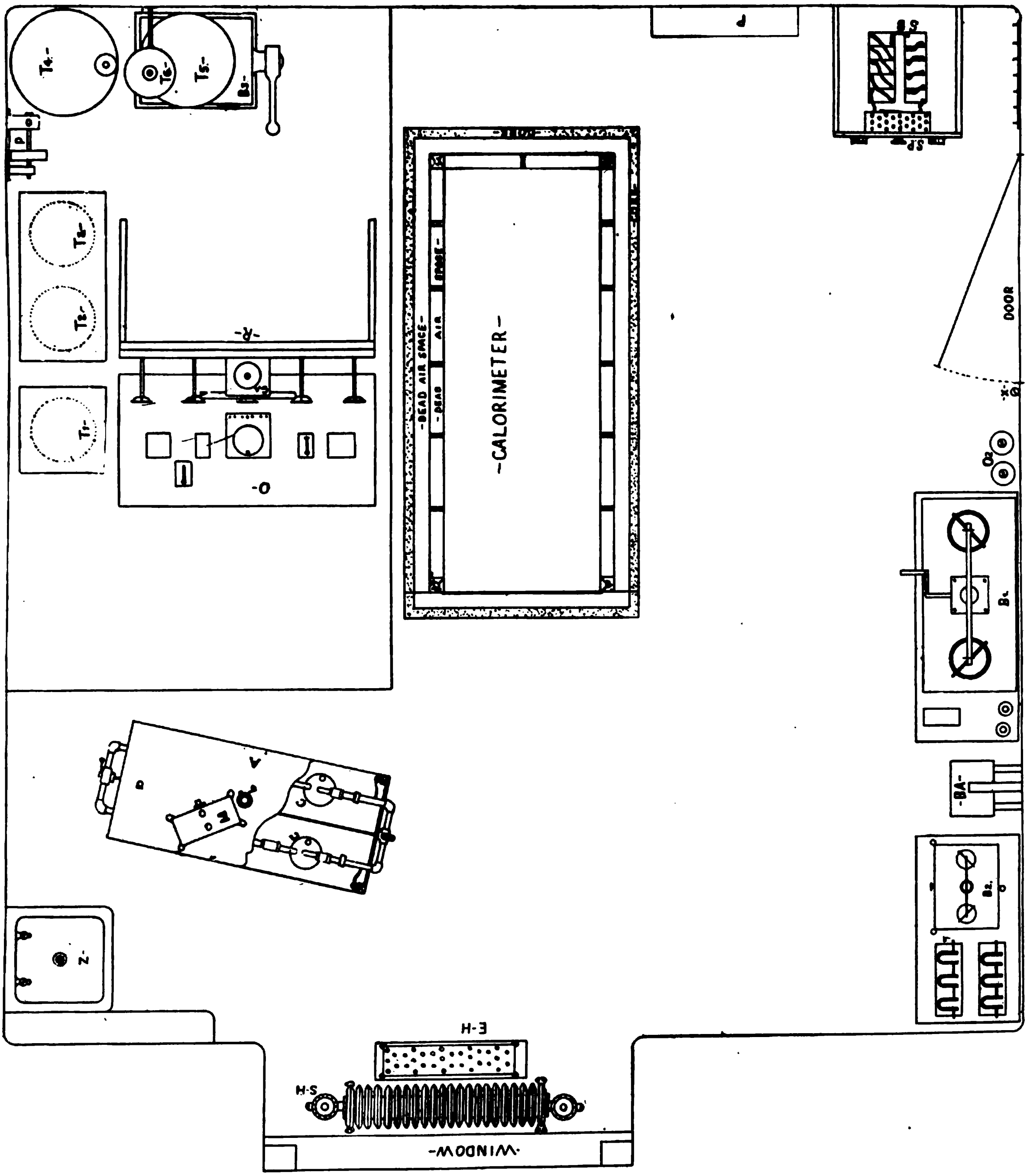

Fig. 3.—The calorimeter room. A, Absorber table. M. Bohr meter. b, Drying tower for air sample drawn through meter. CC, Williams bottles containing sulphuric acid. SH, Steam heater. EH, Electric heater. Z, Sink. O, Observer's table. Ga, Galvanometer. R, Rheostat board. T_1, Gouy regulator tank. T_2, Ice tank for cooling water running through absorber in calorimeter. T_3, Ice tank for water to cool outer copper wall. T_4, Large supply tank. T_5, Tank on platform balance (B_3) for weighing water. T_6, Small tank to hold water from absorber while T_5 is being weighed. p, Pump to lift water from T_4, to constant-level tank near the ceiling. P, Panel box. SB, Edison storage batteries. SP, Charging panel. x, Pyrene fire extinguisher. O_2, Oxygen tanks. B_1, Balance for sulphuric bottles, etc. Ba, Barometer. B_2, Balance for U-tubes.

volume of contained air and magnifies certain errors, but makes the box much more comfortable and apparently gives better results than if the quarters were cramped. The frame (Fig. 4) was made of wood, as previous experience with the small calorimeter in Cornell had shown that the mass of angle iron between the metal walls made the box very sluggish in responding to temperature changes. To prevent warping, which would be disastrous, the best quality white pattern pine was used and the frame allowed to stand for several months before it was shellacked. The outside timbers were 6.35 by 6.35 cm. square and the braces 6.35 by 1.9 cm. All joints were glued and dowelled. The braces were spaced 30.48 cm. apart to give rigidity to the copper walls which are attached to the wood in many places.

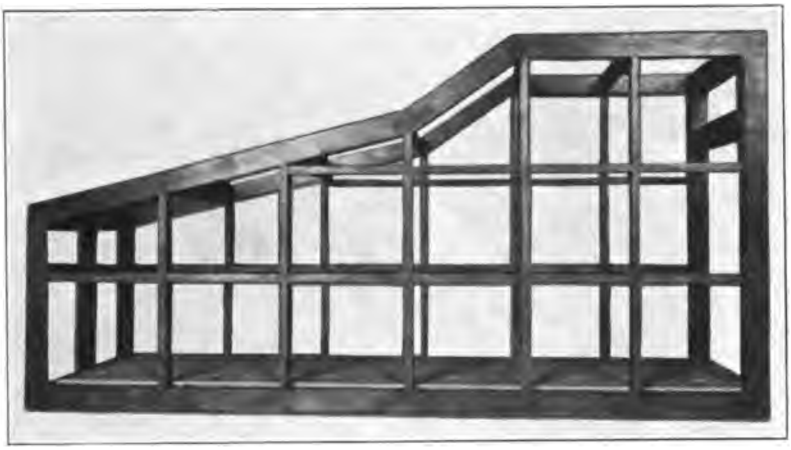

Fig. 4.—Wooden frame of calorimeter with asbestos board as floor.

COPPER WALLS

The inner copper wall (Fig. 5) forms an air-tight box 198.18 cm. long, 76.2 cm. wide, 91.4 cm. high at one end and 45.7 cm. at the other, with a capacity of 1,123 liters. At the head is an opening to serve as a door and on one side an opening for a window.

The wall is made of "16-ounce" sheet copper, tinned on the inside. It is fastened to the inner side of the wooden frame by means of brass angles soldered to the copper and screwed to the wood. The bottom rests on a long slab of asbetos board 9.5 mm. thick.

The outer copper wall (Fig. 6) which is screwed directly on the outer side of the wooden frame, does not come in metallic contact with the inner wall at any place except the rim around the large opening at the head of the box. This outer wall is made of "14-ounce" copper tinned on the outside, and while the joints are soldered they are not necessarily air-tight.

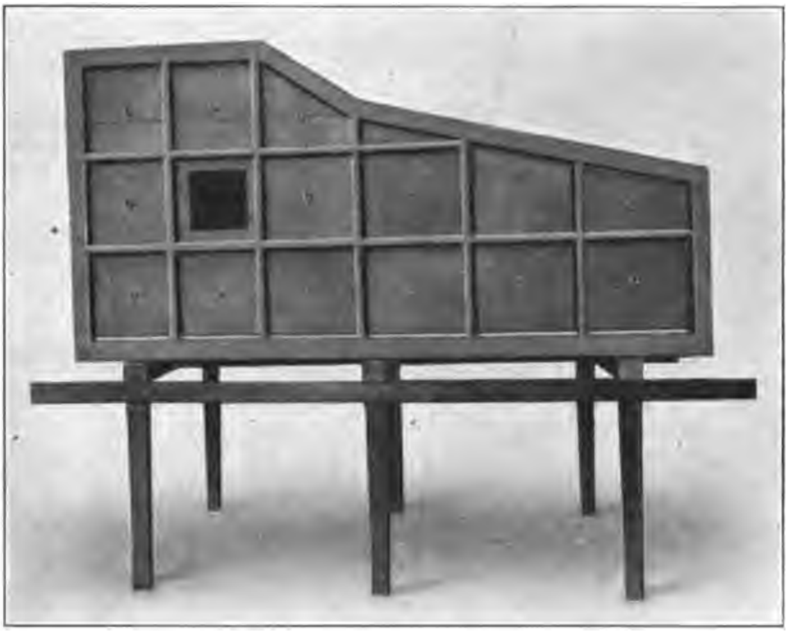

Fig. 5.—Inner copper box with brass thimbles for thermopiles.

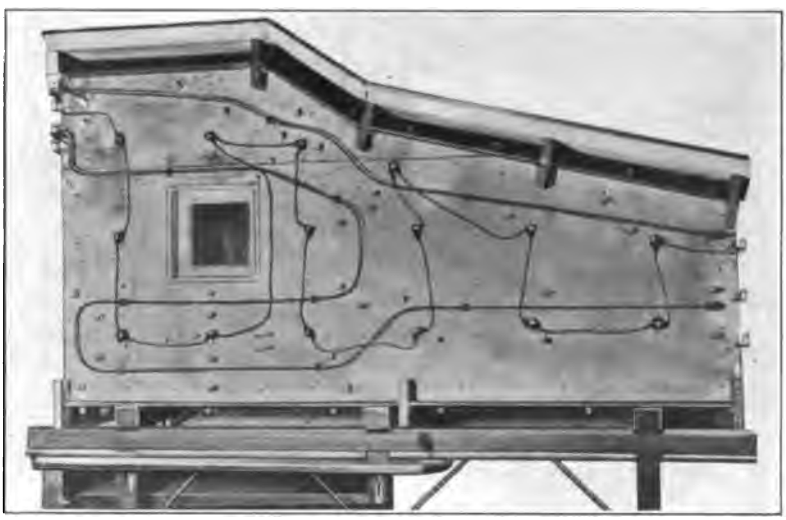

Fig. 6.—Outer copper box with leads connecting thermopiles, pipes for cold water and porcelain insulators for resistance wires. The wires themselves are not shown in the photograph. The top and bottom of the wooden box are in position.

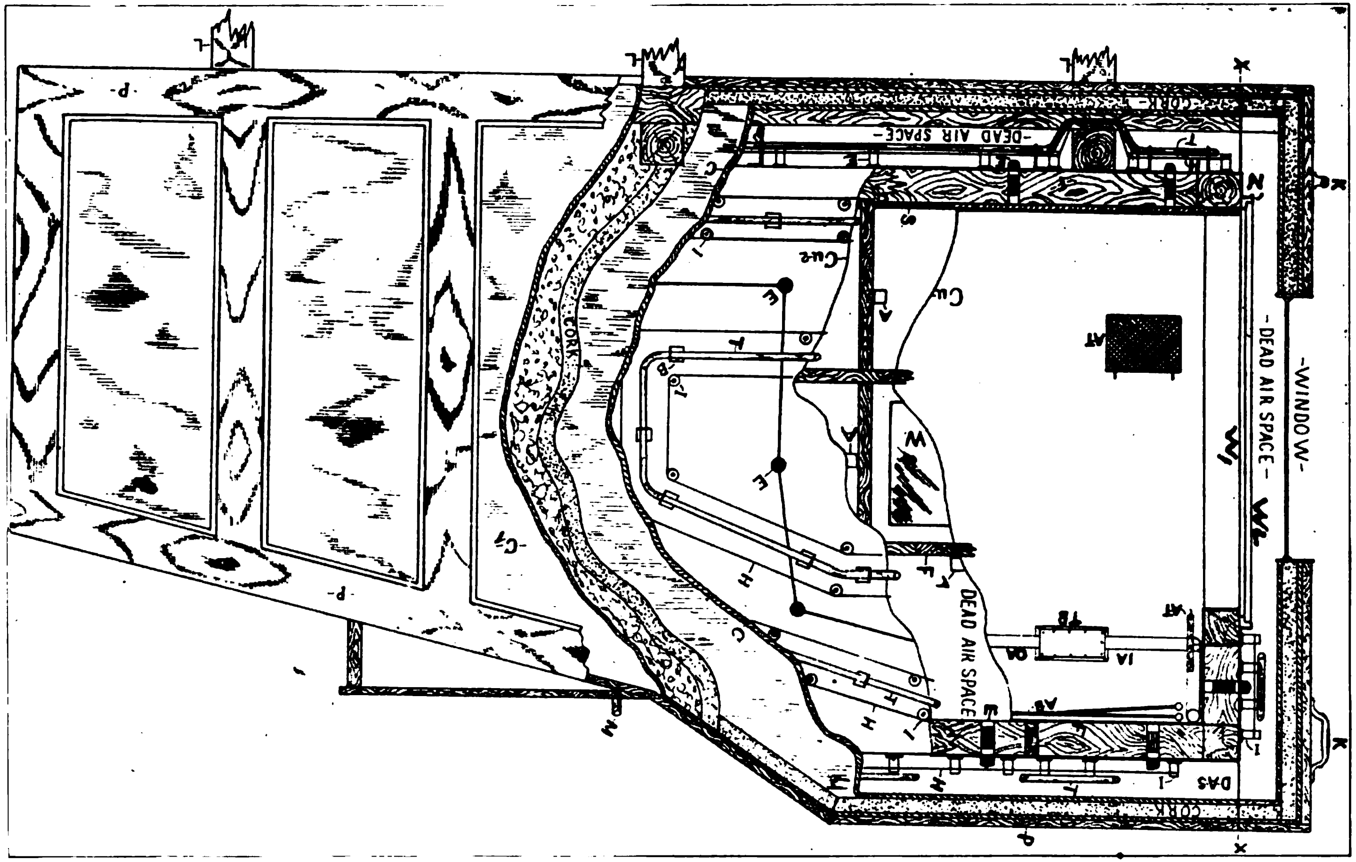

Fig. 7.—Sectional view of the calorimeter. AA, Brass angles fastening inner copper wall to wooden frame. AT, Air thermometer. AB, Heat absorber pipes. BB, Brass angles supporting cold water pipes on the outer copper wall. C, Inner layer of "Compo Board." C_1 Outer layer "Compo Board." Cu, Inner copper wall. Cu2, Outer copper wall. DAS, Dead air space. EE, Thermopiles. F, Wooden frame. H, Resistance wire. I, Porcelain insulators. IA, Ingoing air pipe. K, Handles of wooden panel at head of box removed at line X - X. L, Wooden legs of calorimeter. M, Pipe leading from interior of box to spirometer. N, Copper frame in which are placed glass plates W_1 and W_2. OA, Outgoing air pipe. P, Wooden supports for "Compo Board." S, Asbestos board under floor of calorimeter. TT, Cold water pipe. W, small window.

The braces of the wooden frame divide the dead air space between the walls into compartments about 30.48 cm. square and 6.35 cm. thick. In the center of each compartment is placed a thermopile with four thermocouples in thermal but not in electrical contact with each copper wall. The inner end of this thermopile fits in a brass thimble 25.4 mm. deep soldered to the outer side of the inner wall. The outer end (with its four thermocouples) fits in a brass tube which passes through the outer wall and is closed off from the outside air by P. B. Compound and electric tape.

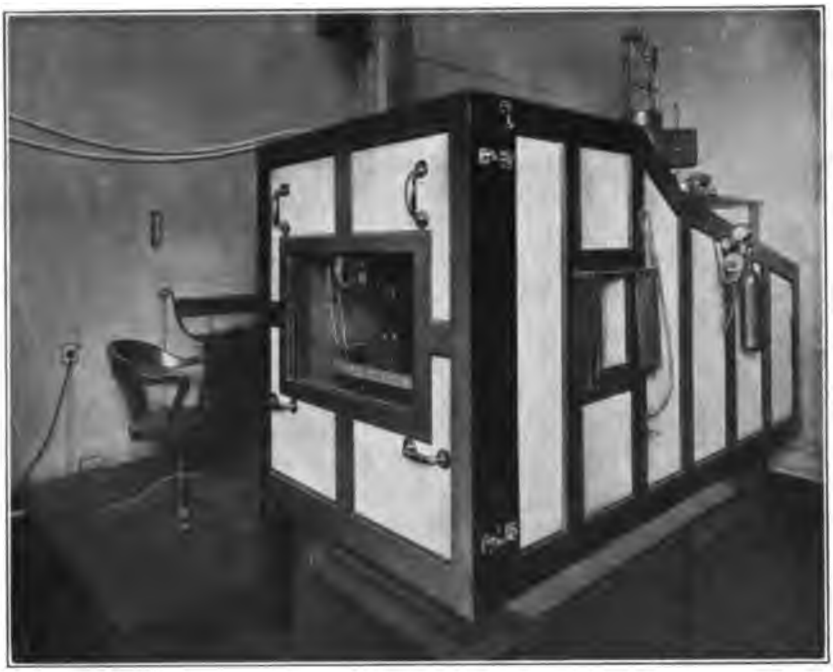

Fig. 8.—Calorimeter with front closed.

In Figure 13 the large opening at the head of the box, measuring 76 by 70 cm., is closed by two glass plates 7.5 mm. thick, each sealed after the subject has entered the calorimeter by means of a mixture of 5 parts bees-wax and 1½ parts Venice turpentine. The small window in Figure 6 is permanently closed by glass plates fastened to the copper walls. There are numerous pipes and electric cables entering the box as will be described later.

On the surface of the outer copper wall are attached the wires connecting the thermopiles. The pipes for cold water are swung on brass angles attached to this surface and the enameled "Therlo" resistance wire is bound on insulators to the same surface, very much as described by Benedict and Carpenter.

INSULATING WALL

Completely surrounding the outer copper wall and separated from it by a space of 7 cm. is the thick wall intended to protect the calorimeter from fluctuations in the room temperature. This is constructed of a layer of pressed cork 2.54 cm. thick, between two layers of "Compo Board," a patented building material made of strips of wood glued between layers of stout paper. This is supported by a framework of white-wood, making panels which are light, yet very effective as heat insulators. The head of the wooden box is provided with a glass window and furnished with handles so that it can be easily removed when the experiment is over and placed on a small shelf on the right of the calorimeter. The frame of this outer box is stained to resemble oak, and the "Compo Board" panels are painted with white enamel. Every effort has been made to make the room and the calorimeter pleasing to the eye, with the result that patients are attracted by the beauty of the apparatus rather than by its resemblance to a coffin.

THE ABSORBER TABLE

The absorber table is so arranged that the air current is switched from one set of absorbers to the other by means of a three-way valve. This works satisfactorily and is much quicker than the old style seat-valves. The sulphuric bottles are larger models of the form described by Williams and hold about 1¼ liters of acid, which will remove every trace of moisture until more than 100 grams has been absorbed. The soda-lime bottles resemble those devised by Benedict,[6] except for a modification of the tube which carries the entering air. This is divided in such a manner that the soda-lime can be packed about a brass pipe, the lower end of which is perforated and the upper end of which reaches almost to the top of the bottle, where it fits snugly in an elbow attached to the stopper. The Crowell blower is the same as the ones used by Williams and Benedict, but a safety device has been attached to prevent accidental reversal of the blower which would have disastrous effects. The two small bicarbonate cans next to the last sulphuric bottle did not remove entirely the acid vapors and it was necessary to place a long cylinder in the vertical pipe which carries the air from the absorber table. This contains about 340 grams of bicarbonate of soda packed between layers of cotton and catches all traces of acid fumes.

The air enters the box in a pipe which ends in a single opening directed just above the subject's head and leaves through a number of small openings in a pipe which runs across the foot of the box. A small electric fan at the lower end of the calorimeter keeps the air well stirred.

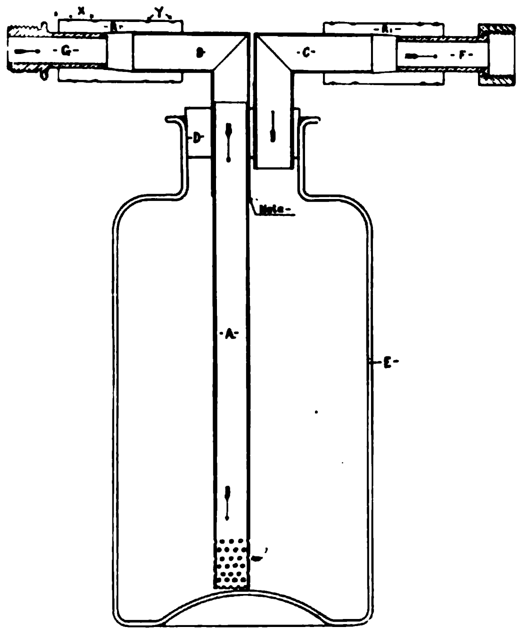

Fig. 9.—Modified soda-lime bottle. A, Brass tube with perforated bottom and top which fits in brass elbow, B. The bottle is filled with A in position and the rubber stopper D with elbows B and C is then forced into neck of bottle. G and F, Brass couplings. R and R_1, heavy rubber tubing. X and Y, Binding wires.

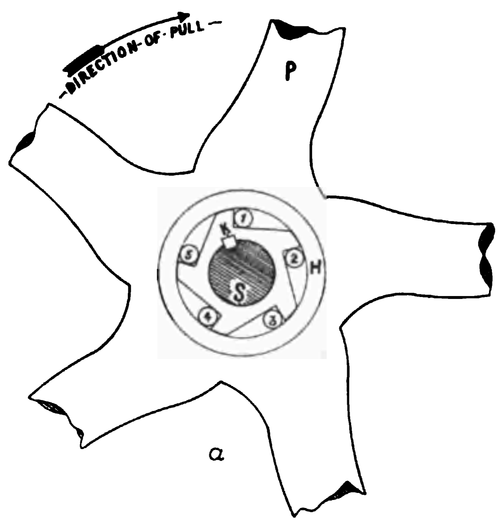

Fig. 10.—Safety device to prevent blower from being reversed. P, Pulley for belt to motor. S, Shaft of blower. H, Hub of wheel. K, Key 1, 2, 3, 4, 5, hardened steel rollers which engage when pulley is running in right direction, but disengage when pulley starts in opposite direction.

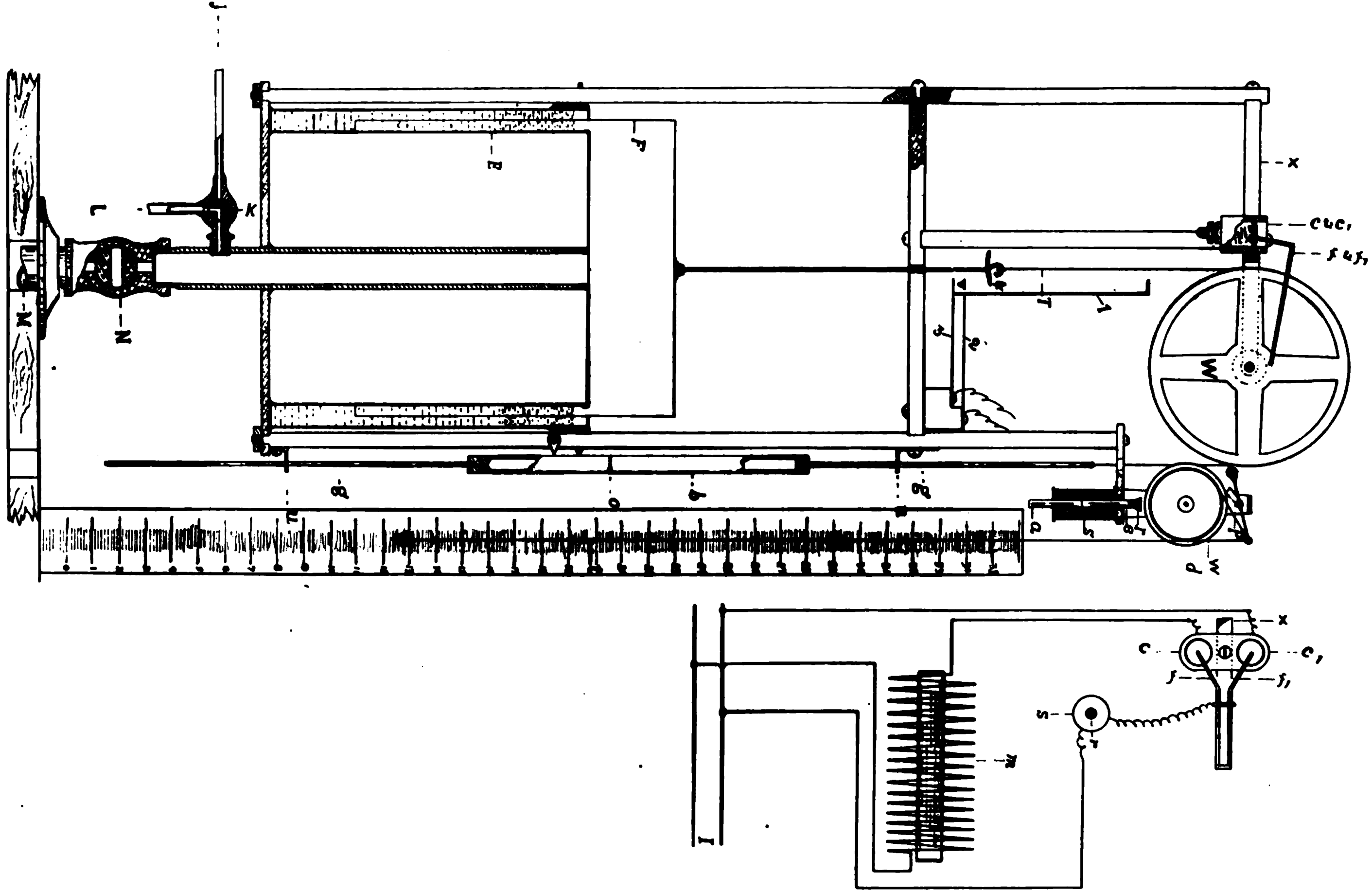

Fig. 11.—Spirometer and Work-Adder. M, Pipe from calorimeter to spirometer. N, two-way valve. J, Small pipe to ingoing air pipe. L, Oxygen inlet. K, Three-way valve arranged to admit oxygen into ingoing air pipe or into spirometer. E, Spirometer tank filled with water. F, Spirometer bell of light copper. T, String supporting bell. W, Wheel supporting bell. b, Counterpoise filled with mercury. gg, Guiding rod fitting loosely in uu. o, Mark on counterpoise. The spirometer is filled at the end of each period until this mark is opposite the pointer. w, Work-adder with toothed edge and cam. d, Drum on which is wound the thread t. P, Small lever with eye through which thread passes. When the thread is pulled downward the cam is lifted. s, Solenoid. r, e, a, Plunger which is raised by solenoid, pressing against edge of work-adder while the spirometer bell is being raised by the admission of oxygen. r, Soft rubber; e, hard rubber; a, iron. x, brass support. c and c_1, mercury cups into which dip f and f_1 when the spirometer bell sinks, making contacts which raise plunger and energize magnet m, thus admitting oxygen. I, Low voltage current corresponding to I, of Fig. 15. 1, 2, 3, 4, Automatic alarm which rings a bell whenever spirometer rises dangerously high or sinks too low. 4, A button on the rod supporting spirometer bell makes contact between 2 and 3 either by raising hook 1, connected with 3, or by depressing the small triangular knob connected with 2.

The spirometer on the top of the calorimeter resembles Benedict's[6] except that it is provided with a work-adder to record movement of the patient and not the total ventilation of the lungs. The bell is made of very light copper, is suspended in water and is carefully counterpoised. The counterpoise is provided with a writing point which records on a smoked paper the movements of the drum. To the wheel at the top is attached a brass arm with two points which dip into mercury cups set at slightly different levels whenever the spirometer bell

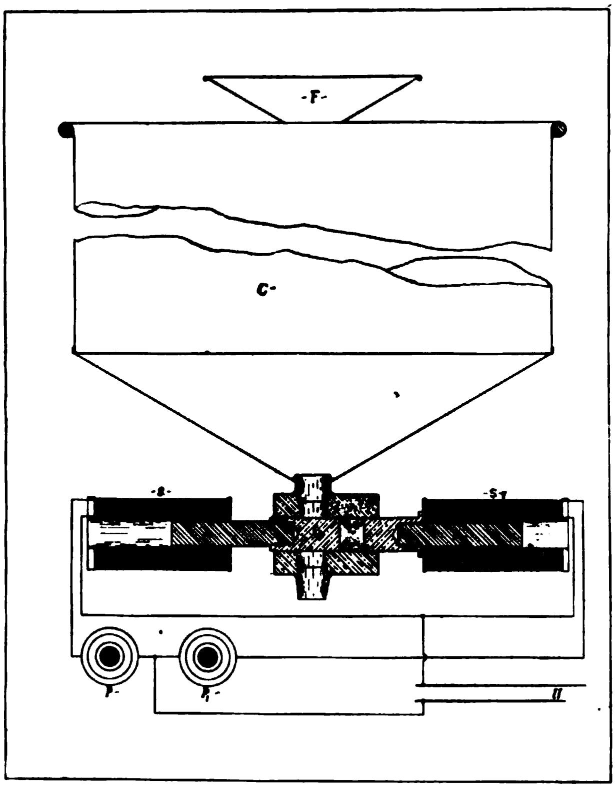

Fig. 12.—Electrical device for shutting and opening valve P. P_1. Push buttons controlling solenoids S and S_1. A and A_1 iron cores attached to brass rod V. Valve is shown closed. When current is passed through S the Rod V will be drawn to the left and the narrow portion seen just under V_1 will come opposite the pipe leading from receiving can G.

sinks below a certain mark. One of these cups operates a magnet which opens the attachment that automatically admits the oxygen. This keeps the spirometer within about one centimeter of the same level unless the subject moves and suddenly heats the air locally. It is remarkable how promptly the spirometer rises when the person within the box makes even a slight movement of a hand or leg. In fact, it makes so delicate a

movement recorder that a Porter work-adder has been attached in such a manner that the downward movement of the counterpoise winds up a thread and the total amount of thread so wound represents the total work done by the patient during that particular period. By standardizing various movements of the body such as turning over or lifting the arm it is possible to gain a fairly accurate idea of the amount of mus-

Fig. 13.—View of open calorimeter. Patient on canvas bed partly in the chamber. On the left can be seen the observer's table and the rheostat board with the galvanometer. The rubber pipes for outgoing and ingoing air lead to the absorber table, a corner of which can be seen on the extreme left. In the background on the right are the storage batteries and charging panel.

cular movement and express it in centimeters of thread, thus obviating the necessity of printing long graphic records. In order to prevent the work-adder from winding up thread while the oxygen is being admitted,

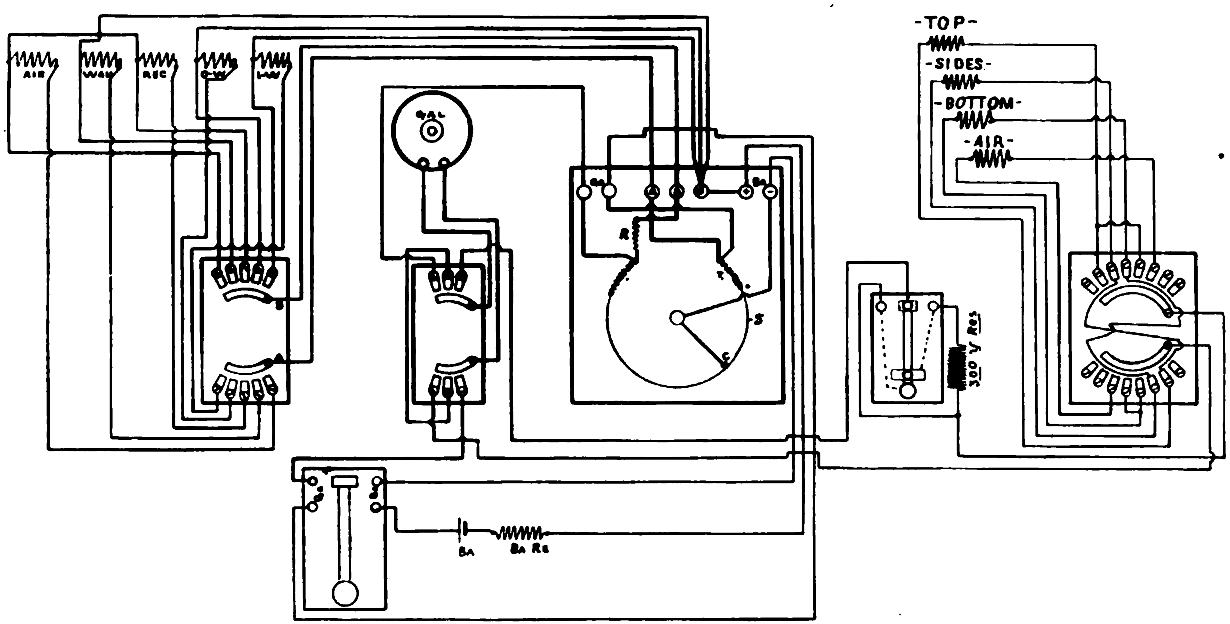

Fig. 14.—Wiring diagram of observer's table. In the center is the Kohlrausch bridge, to the right a tapping key with an arrangement for throwing in 300 ohms resistance when needed. This key is used in reading the thermopiles connected with the switch on the right. To the left of the bridge is a switch for connecting either thermopiles or resistance thermometers with the galvanometer. On the extreme left is the switch for the air, wall, rectal, ingoing and outgoing water thermometers, each of which contains 100 ohms. Since this diagram was made two additional thermometers for surface temperature have been added. In the front of the table is a tapping key.

a solenoid is connected with the second mercury cup into which the brass arm on the wheel dips. This solenoid operates a small plunger which holds the work-adder while the magnet opens the oxygen valve and also maintains its hold for the instant after the oxygen has been shut off, since the spirometer rises somewhat slowly after the admission of oxygen. This solenoid lag, which corresponds to the spirometer lag, is secured by having the second mercury cup filled slightly more than the cup which controls the oxygen magnet.

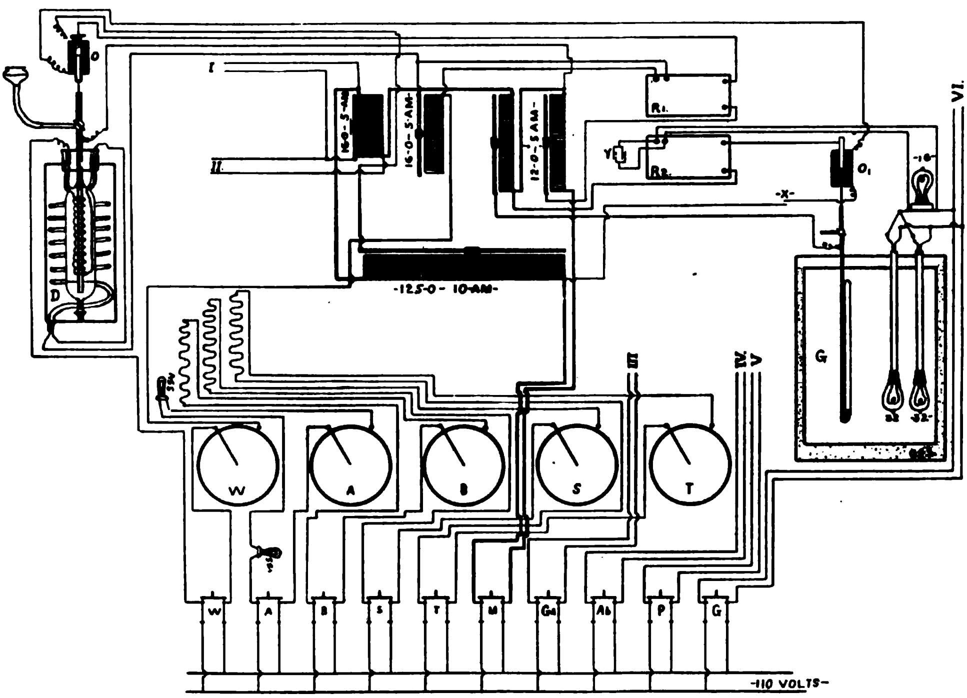

Fig. 15.—Wiring diagram of rheostat board. W, Switch and rheostat to control temperature of ingoing water in water heating resistance, D. A, Ingoing air. B, Bottom of calorimeter. S, Sides. T, Top. Ga, Galvanometer lamp. Ab, Motor on absorber table. P, Motor for pump. G, Lamps in Gouy regulator. M, Miscellaneous parts connected with tube rheostats. O, O_1, Solenoid agitators lifting and dropping platinum contacts with mercury in Gouy and current regulator as the contact is made and broken mechanically at x. R_1, Relay for current regulator. R_2, Relay to control heating of lamps in Gouy.

The heat-absorbing system is the same as that described by Williams, the Gouy regulator and Williams' water heating resistance and current regulator giving very satisfactory results. The water coil suspended from the roof of the calorimeter has, however, been wound with brass "jack chain" to increase its absorbing surface. From this coil the water runs to the weighing tank on the platform of a "silk scale"

which is sensitive within 10 grams. The flow of water was formerly cut off by hand at the end of each period, but this is now done by a pair of solenoids controlled by the operator at the observer's table, thus reducing the staff by one man. The stream of water runs constantly through a can which has the capacity of 10 liters, and is provided at its lowest point with a valve that is opened and shut by the pair of solenoids above mentioned. At the end of a period the valve is shut and the water collects in the can while the tank is being weighed. After the weighing is finished the valve is opened and the water runs once more into the tank.

RHEOSTAT BOARD AND OBSERVER'S TABLE

The marble rheostat board and the observer's table resemble closely those described by Williams. This rheostat board, the panel box, charging panel for the storage batteries, conduits, wires, etc., were installed by the Electric Construction Supply Company after specifications kindly drawn up for us by the Department of Water Supply, Gas and Electricity of New York City. Directly above the rheostat board is mounted a galvanometer of the d'Arsonval type, provided with prisms so that the ascending ray of light from the lamp below is reflected from the mirror of the galvanometer downward to a scale just above the table. (Siemans and Halske.) This vertical mounting with scale that can be read by daylight saves a great deal of room. The galvanometer is braced securely and does not vibrate. To protect it from the dust it is covered with a thin copper hood. The resistance of the moving system is 45 ohms and there is a ballast resistance of 200 ohms in series, which, however, is not used.

Most of the precision switches used were furnished by Siemans and Halske, Catalogue Number 17327. One of similar design was made in our own shop. A new device which has given great satisfaction has been introduced into the switch connecting thermopiles with galvanometer. At the start of the experiment, or at any other time when the temperature differences between outer and inner walls are large, a resistance of 300 ohms is kept in series. As soon as the calorimeter is in balance a button on the switch is turned and the resistance short-circuited, making the adiabatic control extremely delicate. The Kohlrausch bridge provided by the Leeds and Northrup Company of Philadelphia is similar to the one described by Williams. The 60-step rheostat for controlling the temperature of the ingoing water and the four 45-step rheostats controlling that of the ingoing air, bottom, sides and top of the outer copper wall, were made by the Simplex Heater Company of Cambridge, Mass. They are mounted on the back of the board with their handles projecting through the board to the observer's

table. Just above them on the back of the marble slab are the five tube rheostats (Siemans and Halske) used to cut down the current to various small pieces of apparatus. On the front of the board are the two relays, one for the Williams water heating resistance and current regulator and the other for the Gouy regulator.

The thermopiles between outer and inner copper walls are arranged in three groups, thirty-two on the top, thirty on the sides and twelve on the bottom, the area covered by each group being warmed by a strand of enamelled "Therlo Wire," No. 24 B & S gauge, whose temperature is controlled by one of the step rheostats.

One thermopile is arranged with one end in the outgoing air current and the other in the ingoing air. The temperature of the latter is adjusted to that of the former by means of a step rheostat and two 55 volt lamps. A similar rheostat controls the temperature of the ingoing water by means of the water heating resistance.

THERMOMETERS

All thermometers contain 100 ohms resistance in nickel or platinum wire and are made on the three-lead system, being read on the same galvanometer used for the thermopiles. The water thermometers made by Leeds and Northrup are similar to those constructed by them for the automatic calorimeter of the Department of Agriculture. They are described in the Leeds and Northrup catalogue (Bulletin 811) and also by Dickinson and Mueller[7] of the United States Bureau of Standards. In our hands they have been most satisfactory, since they are more accurate, easier to calibrate, and easier to read than mercurials. The Leeds and Northrup air thermometer, similar to that used by Williams, is in eight divisions scattered over the inside of the box so as to give the average temperature of the air. They are connected in series by copper wire covered with rubber and a casing of lead, a combination made especially for us which has given good service. The wall thermometer consisting of eight divisions in series was made in this laboratory. Each division was made of No. 38 double silk covered nickel wire wound around a strip of mica and held 2 or 3 mm. from the inside of the inner copper wall. Over this was soldered a shallow copper box so that the resistance wire would lie in a small air space completely surrounded by metal at the temperature of the wall.

The rectal thermometer is of a new design made to respond more rapidly to changes in the temperature than the old type in which the resistance wire was surrounded by a jacket of dead air. The nickel wire with its double silk covering is wound on a small piece of ivory

7. Dickinson and Mueller: New Calorimetric Resistance Thermometers, Bull. Bureau Standards, 1913, ix, 483.

and dipped in a round ended silver tube filled with molten Wood's fusible alloy at a temperature of 96 C. This is solidified by dipping in water, thus forming direct metallic contact between the outside of the silver tube and the insulated wire. The leads from the thermometer are enclosed in a soft rubber tube. The surface thermometers are made of flat circular buttons of ivory 25 mm. in diameter and 5 mm. thick. One side of the button is hollowed out to a depth of 3 mm., the edges being filleted. On the bottom of this depression is wound concentrically the resistance wire. On this is poured the molten Wood's metal until it is flush with the original level of the ivory. Two of these units are used in series in each of the two surface thermometers. They are strapped to the skin with adhesive plaster and covered with a pad of cotton wool about 20 cm. in diameter and 4 cm. thick, this also being held in place with adhesive plaster.

The air thermometers were calibrated by the makers and the wall thermometers made to contain exactly the same resistance. Since they are used only to denote relative changes in temperature, a more exact calibration is not necessary. The rectal, surface and water thermometers are standardized several times a year by means of very accurate mercurials, certified by the Physikalische Technische Reichsanstalt. When calibrating them one notices that the electric thermometers all respond to temperature changes much more quickly than the mercurials.

The flexible rubber covered leads from the surface and rectal thermometers and the lead covered wires from the wall and air thermometers are carried to a ten-wire cable which perforates the calorimeter walls and is distributed on a hard rubber plate attached to the calorimeter and thence carried to the switches on the observer's table. The high tension currents from the calorimeter pass to a small hard rubber plate inside the box, thence in a separate strand cable to a slate board outside the calorimeter, and thence to the rheostat board. This cable carries leads for the telephone, electric fan and for the resistance coil used in electric checks.

ACCESSORY APPARATUS

The telephone, which has been made as light as possible, is seldom used, since the muscular work involved in telephoning is enough to affect seriously the results in rest experiments. The small electric fan placed in a corner at the foot of the calorimeter stirs the air thoroughly and allows one to get a good sample by drawing off ten liters through the large Bohr meter attached to the outgoing air pipe. The fan is run by the Edison storage batteries, giving off approximately 4.5 calories an hour, the exact amount being determined once an hour by a voltmeter and ammeter.

On the right side of the subject is a small glass shelf for the weighed urine bottles which, after each voiding, are placed on a spring balance that can be read through the window. Two small brass tubes are led through the wall of the calorimeter just below the small window. One acts as an emergency vent to prevent a positive or negative pressure at the beginning or end of an experiment when the ventilation is stopped. To the other is attached the Bowles stethoscope, which is strapped over the apex of the heart so that an observer outside can count the pulse at frequent intervals.

The inside of the calorimeter is formed by the polished tinned copper, the roof being almost hidden by the longitudinal absorber pipes wound with brass "jack chain." The calorimeter is wide enough for a man to turn comfortably from side to side, high enough at the foot to allow him to cross his legs and high enough at the head to allow him to sit upright.

THE BED

The bed in its present form is the result of much experimentation. The frame is made of varnished oak raised at the head so that the top is 12.7 cm. from the floor of the calorimeter while it is raised only 8.2 cm. at the foot. This allows for the sag of the waterproof canvas laced in the frame and keeps the subject 2 to 3 cm. from the copper floor. At the head is a back-rest with a piece of water-proof canvas, which is usually supplemented by a soft pillow. The bed is mounted on a pair of skids so that it can be pushed from the stretcher into the box. The canvas has proved to be much more comfortable than the springs and blankets formerly employed and has the advantage of absorbing very little water vapor. The varnished wood absorbs some water, the necessary clothing of the patient a great deal more, while the polished walls absorb only a minimum.

ELECTRIC AND ALCOHOL CONTROL EXPERIMENTS

The calorimeter has been tested repeatedly by dissipating known amounts of heat in resistance coils and by burning known amounts of alcohol. The apparatus and procedure used correspond almost exactly with those described by Williams and are similar to those previously used by Atwater and Benedict and by Benedict, Riche and Emmes.[8] In calculating the latent heat of the evaporation of water we have adopted the figures of Smith[9] and have given the latent heat the value of 0.584 large calories per gram of water evaporated at 23 C., the usual experimental temperature.

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8. Benedict, Riche and Emmes: Control Tests of a Respiration Calorimeter, Am. Jour. Physiol., 1910, xxvi, 1.
9. Smith, A. W.: Heat of Evaporation of Water, Physical Review, 1907, xxv, 145.

TABLE 1.—ALCOHOL CHECKS *

Date and Per Cent. Alcohol by Weight	Hour	Heat				Oxygen			Carbon Dioxid			Water			R. Q. Theory, 0.667
		Alcohol Burned, Gm.	Theory, Cal.	Found, Cal.	Error, Per Cent.	Theory, Gm.	Found, Gm.	Error, Per Cent.	Theory, Gm.	Found, Gm.	Error, Per Cent.	Theory, Gm.	Found, Gm.	Error, Per Cent.	
3/8/13 92.28	1	10.14	66.25	64.52	−2.6	19.53	19.11	−2.2	17.90	17.81	−0.5	11.76	12.92	+9.8	0.662
	2	10.08	65.86	65.86	±0.0	19.41	18.08	−6.9	17.79	18.18	+2.3	11.69	11.82	+1.1	0.715
	3	9.85	64.62	64.29	−0.0	19.06	19.17	+0.6	17.46	17.44	−0.1	11.47	11.56	+0.8	0.662
	4	9.43	61.61	60.49	−1.8	18.16	17.99	−0.8	16.65	16.48	−1.0	10.94	11.10	+1.4	0.666
Average	..	......	64.52	63.79	−1.1	19.04	18.59	−2.4	17.45	17.48	+0.2	11.47	11.86	+3.4	0.676
4/30/13 91.60	1	8.42	54.60	56.06	+2.7	16.09	16.61	+3.2	14.75	14.73	−0.1	9.75	10.29	+5.5	0.644
	2	8.19	53.04	52.59	−0.8	15.65	15.43	−1.4	14.35	14.30	−0.4	9.48	10.01	+5.6	0.674
	3	8.14	52.79	51.86	−1.7	15.56	15.39	−1.1	14.26	14.37	+0.8	9.42	9.94	+5.5	0.680
	4	8.04	52.14	51.37	−1.6	15.37	15.23	−0.9	14.08	13.82	−1.8	9.31	9.55	+2.5	0.660
Average	..	......	53.14	52.97	−0.3	15.67	15.67	±0.0	14.36	14.31	−0.4	9.49	9.95	+4.8	0.665
10/14/13 90.96	1	12.24	78.53	76.50	−3.0	23.22	23.20	−0.1	21.29	21.34	+0.2	14.15	14.73	+4.1	0.669
	2	12.36	79.66	80.48	+1.1	23.45	24.82	+5.8	21.50	21.98	+2.3	14.29	14.83	+3.7	0.644
	3	11.86	76.37	73.78	−3.3	22.50	20.55	−8.6	20.63	19.98	−3.0	13.71	13.53	−1.4	0.707
Average	..	......	78.27	76.92	−1.7	23.06	22.86	−0.8	21.14	21.10	−0.2	14.05	14.36	+2.2	0.673
2/2/14 91.18	1	9.22	59.52	59.82	+0.5	17.54	17.62	+0.5	16.07	15.65	−2.7	10.43	10.85	+4.0	0.646
	2	9.29	59.97	61.29	+2.2	17.67	16.78	−5.0	16.20	15.75	−2.8	10.51	10.71	+1.9	0.682
	3	8.59	55.45	56.23	+1.5	16.84	15.98	−2.2	14.98	15.07	+0.6	9.72	10.30	+6.0	0.686
	4	9.70	62.62	64.05	+2.3	18.45	18.24	−1.2	16.91	16.82	−0.5	10.97	11.32	+3.2	0.671
Average	..	......	59.39	60.35	+1.6	17.50	17.16	−1.9	16.04	15.82	−1.3	10.41	10.80	+3.8	0.671
3/19/14 91.18	1	10.41	67.20	67.34	+0.2	19.80	19.41	−2.0	18.15	18.23	+0.4	11.77	12.02	+2.0	0.683
	2	11.02	71.14	69.43	−2.4	20.96	19.33	−7.7	19.21	18.14	−5.6	12.46	12.13	−2.6	0.663
	3	10.89	70.30	70.36	+0.1	20.71	19.53	−5.7	18.99	18.61	−2.0	12.32	12.62	+2.5	0.693
	4	10.04	64.81	66.29	+2.3	19.10	20.13	+5.4	17.50	17.75	+1.4	11.36	11.96	+5.2	0.641
Average	..	......	68.36	68.36	±0.0	20.14	19.60	−2.6	18.46	18.18	−1.5	11.98	12.18	+1.7	0.675
Total....	..	......	1216.72	1212.61	−0.33	358.56	325.60	−1.69	328.67	326.45	−0.68	215.52	222.18	+3.09	Av. 0.672

* All periods one hour long.

It has seemed advisable to publish all the electric and alcohol checks made with the calorimeter. In publishing control tests the results are much more striking if one selects only the best and leaves out those in which the agreement is not close. This method expresses only the minimum error while the things we really need to know are the average, maximum and total errors. The total error shows the accuracy of the method, the maximum error may occur in the course of any experiment, while the average error is with us always. The minimum error

TABLE 2.—ELECTRIC CHECKS

Date	Length of Period, Min.	Calories, Theory	Calories, Found	Per Cent. Error
3/4/13	60	72.25	73.19	+1.2
	60	72.25	72.19	+0.0
Average	..	72.25	72.69	+0.6
4/5/13	60	80.78	77.26	−4.4
	60	80.78	79.31	−1.8
Average	..	80.78	78.29	−3.1
10/18/13	30	41.74	42.15	+1.0
	30	41.74	41.56	−0.4
	30	41.74	41.25	−1.2
	30	41.74	41.10	−1.5
	30	41.74	41.85	−0.8
Average	..	41.74	41.49	−0.6
10/22/13	60	83.98	83.98	±0.0
	60	83.98	83.83	−0.2
	60	83.98	84.02	+0.0
	60	83.98	83.84	−0.2
Average	..	83.98	83.92	−0.1

Date	Length of Period, Min.	Calories, Theory	Calories, Found	Per Cent. Error
11/28/13	60	78.22	77.15	−1.4
	60	78.22	77.62	−0.8
	60	78.22	78.67	+0.6
Average	..	78.22	77.81	−0.5
1/26/14	60	76.92	75.86	−1.4
	60	76.92	77.41	+0.6
	60	76.92	77.88	+1.3
	60	76.92	77.24	+0.4
Average	..	76.92	77.10	+0.2
5/11/14	60A	78.71	80.03	*
	60B	78.22	75.18	....
	30C	39.07	41.35	....
Total....	150	196.00	196.56	+0.3
Total of all checks	..	1589.02	1583.42	−3.5

* A, B, C. Temperature changes of wall of calorimeter: A, +0.06 C.; B, −0.73 C.; C, −0.05 C. Test to verify hydrothermal equivalent.

is a joy to behold, but it does not occur with the regularity inferred by the prominence it is usually given. If, for instance, we should publish only the electric check of October 22 with an hourly error of 0.2 per cent., and the alcohol check of April 30, in which the total errors in the measurement of heat, oxygen and carbon dioxid are all less than ½ of 1 per cent., we should give a false impression of accuracy. This test shows that the calorimeter is capable of measuring heat, oxygen and carbon dioxid with a maximum error of 1.8 per cent. in three consecutive hours. Even better results could be obtained if greater care were taken to secure an even combustion of alcohol. On the other

hand, the errors which can occur in hourly periods and in whole experiments are shown in Table 3. The average error has been obtained by multiplying each per cent. of error by the number of times it occurs and dividing the total by the number of periods. In the whole series of experiments of three or four hours' duration the average error for heat is 0.9 per cent., for oxygen 1.6 per cent. and for carbon dioxid 0.6 per cent., while for the individual hours the error is 1.2 per cent., 3.2 per cent. and 1.6 per cent., respectively. The total error in all the

TABLE 3.—SUMMARY OF ERRORS IN ELECTRIC AND ALCOHOL CHECKS

Per Cent. Error	Average of Whole Experiment				Individual Hours			
	Cal.	O_2	CO_2	H_2O	Cal.	O_2	CO_2	H_2O
0..............	5	1	3	..	10	1	5	..
1..............	4	1	1	..	15	7	5	4
2..............	2	2	1	2	9	3	5	2
3..............	1	1	..	1	4	1	3	4
4..............	..	..	..	1	1	..	..	3
5..............	..	..	..	1	..	2	..	1
6..............	..	..	..	..	..	2	1	4
7..............	..	..	..	..	..	1	..	..
8..............	..	..	..	..	..	1	..	..
9..............	..	..	..	..	..	1	..	..
10..............	..	..	..	..	..	..	..	1
Total number of experiments or hours..........	12	5	5	5	39	19	19	19
Average error...	0.9	1.6	0.6	3.2	1.2	3.2	1.6	3.7
Total error......	—0.33	—1.69	—0.68	+3.09				

electric and alcohol checks is: heat, — 0.32 per cent., O_2 — 1.69 per cent., CO_2 — 0.68 per cent. The total error in the water is + 3.09 per cent.

The electric checks show a smaller error in the measurement of calories than the alcohol, since the dissipation of heat is much more uniform. It is difficult to secure an even flow of alcohol to the burner and the larger errors in the oxygen determination are due to irregularities in the flow during the last five minutes of the period. If a slight negative pressure develops within the box toward the end of the period, alcohol is sucked into the burner causing the flame to flare up

and expand the air before the air thermometers record the rise in temperature. This causes an error in the oxygen calculation which, as the tables show, is usually corrected the next hour. With a trained human subject the production of heat and carbon dioxid and the absorption of oxygen are more regular than in the case of an alcohol check and the error presumably not so large. The cause for the negative total error in the measurement of heat, O_2 and CO_2, is not clear, but one cannot help suspecting that a slight absorption of water by the alcohol and a slight evaporation as the alcohol drops from the bottle into the buret may account for most of the error. In experiments on man there is another factor which reduces an error in the measurement of oxygen or carbon dioxid considerably. In calculating the indirect calorimetry the factor by which the oxygen or carbon dioxid is multiplied changes with the respiratory quotient and it happens that a plus error in measurement of the gas is partially offset by a minus change in the factor. This change reduces the error to an extent varying between one-fifth and three-quarters of its original size, unless the errors in both gases are in the same direction, leaving the quotient unaltered. The accuracy of the calorimeter has also been demonstrated by the close agreement of the methods of direct and indirect calorimetry. This will be taken up in detail in the paper on normal controls, but at this point it may be said that in a total measurement of 4,577 calories the two methods agreed within 0.17 per cent., and that in 26-hourly periods on the normal control most carefully studied, the agreement was within 5 per cent. in seventeen of the hours.

In spite of the fact that some of the errors published in the table are larger than those published in connection with other types of apparatus, we feel justified in believing that the Sage calorimeter is the most accurate and most reliable instrument of its size used in the study of the respiratory metabolism. The table includes all the alcohol and electric checks, good, bad and indifferent, made during the period when the machine was used for experiments. The only ones left out are those made at the beginning of the season while the apparatus was being put in order, and actual work was never begun before obtaining a check good enough to publish. To the best of our knowledge this method of publishing all the tests has never been used in connection with other types of respiration apparatus, and we have no detailed information as to their average, maximum and total errors.

It is to be regretted that we have not been able to make long electric tests to determine the hydrothermal equivalent of the calorimeter. The storage batteries are not powerful enough to furnish current for more than four hours in addition to the preliminary period of 30 to 40 minutes, and we have never felt justified in using the house current

with its variations in voltage. Numerous short tests showed that the hydrothermal equivalent was very close to 19 liters of water, and this figure gave results within 0.3 per cent. in the check of May 11 with a large temperature change in the second hour. Incidentally, the advantage of a wooden frame is shown by the rapidity with which the box responded to this temperature variation.

DETERMINATION OF WATER ELIMINATION

In all types of respiration apparatus the measurement of the water elimination has presented great difficulties. This was studied in detail by Benedict, Riche and Emmes, who found that long experimental periods were required to obtain accurate results. The interior of the Sage calorimeter is tinned and polished and there is very little woodwork and cloth, but still a considerable amount of moisture can be retained within the box. In alcohol checks with a water production of only 10 to 14 grams an hour the air becomes dryer and dryer, and this moisture is given off during the whole test, making uniformly a plus error. In experiments on normal men the water elimination is about twice this amount and the percentage of moisture changes but little from hour to hour. In patients who have a tendency to sweat, the water given off may amount to 35 to 40 grams an hour, and there is a tendency for the percentage in the air to increase steadily and finally reach the point of saturation. We should expect a plus error in the determination as the air becomes dryer, a minus error as the percentage of moisture increases, and no error while equilibrium is being maintained. After the first hour of an experiment on man it seems fair to expect an error of less than 5 per cent., except in extreme cases of sweating. More accurate results could be obtained only by removing all wood-work, stripping the man naked and increasing the ventilating current. This would involve such artificial conditions that the results would be worthless.

ADAPTABILITY OF CALORIMETER

By carefully controlling the rate of flow and the temperature of the water in the heat-absorber it is possible to adapt the calorimeter to wide variations in the heat production of the subjects. For example, on April 23, 1914, an experiment was made on a cretin with an average heat production of 26 calories an hour. The next day the subject was a patient with exophthalmic goiter, whose heat production averaged 107 calories. In one case the methods of direct and indirect calorimetry agreed within 0.2 per cent., and in the other within 0.7 per cent. It has also been possible to adapt the calorimeter rapidly to changes in the heat production from hour to hour by changing the temperature of the

ingoing water and in extreme cases by changing the rate of flow at the beginning of a period.

It has been possible in a long series of experiments for two men to take all the readings and make all the calculations in hourly periods. Three men can handle the apparatus with ease during the trying experiments, and most of the alcohol checks, which are much more difficult, have been made with only three in the room. As a rule, the staff arrives shortly before nine o'clock in the morning, makes a three-hour experiment, gets everything in readiness for the next day and leaves the calorimeter room about three or four o'clock in the afternoon. It has been possible, on occasions, to make six experiments in a week. The calorimeter has been very seldom out of commission. Between October 13, 1913, and May 18, 1914, it was possible to make 113 experiments on man and eight alcohol and electric checks.

SUMMARY AND CONCLUSIONS

The original Atwater-Rosa respiration calorimeter with the improvements added by Benedict, Williams and others has been adapted for clinical study in Bellevue Hospital. The form of the apparatus makes it perfectly comfortable for patients. The accuracy is such that in observations lasting three or four hours the heat production, carbon dioxid elimination and oxygen consumption as determined by alcohol and electric tests can be measured with an average error of 0.9 per cent., 0.6 per cent. and 1.6 per cent., respectively. In periods one hour long the average error for heat measurement was 1.2 per cent., for carbon dioxid 1.6 per cent. and for oxygen 3.2 per cent.

The calorimeter never needs more than three men for its operation, and two men have repeatedly made all the readings and all the calculations in hourly periods.

CLINICAL CALORIMETRY

THIRD PAPER

THE ORGANIZATION OF A SMALL METABOLISM WARD*

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All investigators who have attempted to carry on metabolism experiments in hospitals have experienced more or less difficulty in the administration of the diets and the collection of the excreta. The necessity for a special metabolism ward became evident as soon as it was decided to build a respiration calorimeter in Bellevue Hospital. Through the generosity of the trustees of the hospital and the attending staff of the Second Medical Division a small ward holding four or five beds was placed in charge of the medical director of the Russell Sage Institute of Pathology,[1] who was also one of the junior members of the attending staff of the hospital. He is directly responsible to the attending physician for the welfare of the patients, and there has always been a spirit of active cooperation between the small metabolism ward and the large medical wards of the service.

The calorimeter room described in the preceding paper[2] is located on the same floor as the male medical wards of the Second Division in the new Medical Pavilion. The side hall, used as an entrance to the calorimeter room, has been partitioned off to make a small diet kitchen. Next to this is a well lighted ward of four beds used almost exclusively for patients whose metabolism is the subject of active investigation.

The patients are cared for by three graduate nurses, trained in metabolism work and paid by the Institute. The success of the ward is in large measure due to the faithful and intelligent work of the head nurse, Miss Estelle Magill, and her two assistants. They have used the same care in the preparation of food and the collection of excreta that is used in the laboratory and the effort has constantly been made to keep the error within 1 per cent. In order to maintain a high degree of accuracy and at the same time a high standard of nursing it is necessary for the three nurses to devote their whole time to the ward of only four patients. Orderlies, the greatest source of error in metab-

* From the Russell Sage Institute of Pathology in affiliation with the Second Medical Division of Bellevue Hospital, New York.

1. Dr. Eugene F. DuBois.
2. Riche and Soderstrom: See p. 13.

olism work, are excluded from the ward and patients are never allowed in the hospital dining room or kitchen, and only the most trusted are permitted to leave the room at all. These precautions are necessary in order to afford the certainty that the twenty-four-hour specimens of urine are complete and that the patients have not smuggled in outside food. Patients are not allowed out of sight of the nurse in charge for more than a couple of minutes at a time.

The food supplied to patients in the metabolism ward is all prepared by the special nurses, who have become so skilled in the preparation of the various dishes that they can even make one-sided diets attractive. In fact, the patients enjoy the cooking so much that they are sent to their homes or to the general hospital ward with difficulty This is a matter of importance when one desires to keep interesting cases under observation. The foods are prepared as often as possible from raw materials whose composition is determined from time to time. Milk and cream have been of fairly constant composition, as the analyses over a period of several years have shown.

By applying some of the principles of business efficiency, the work has been made a great deal easier. The dry cereals, eggs, bacon, etc., are weighed in white enamel dishes and bowls of known weight marked with serial numbers. Milk and cream are measured in measuring cylinders and added to these dishes in which the food is baked, fried or boiled. The dishes with the cooked food are then taken directly to the patient and if by any chance he should leave some of the food it is an easy matter to weigh it back. Egg whites and yolks are weighed separately. Sugars, salt, cocoa, butter, etc., are put up in packages of known weight by the night nurse to save time during the day.

When a patient first enters the ward the nurses spend a couple days in investigating his dietetic limitations and his dislikes, a matter of great importance. A diet such as the following, for example, is then ordered: 3,000 calories, 15 grams nitrogen, ½ non-protein calories in fat, ½ in carbohydrate. The nurses then work out a diet which will fulfil the specifications and at the same time be agreeable to the patient. Often by careful work it is possible to educate a patient to a diet that he could not otherwise tolerate. We cannot too strongly emphasize the need of individualization aided by good cooking in experimental metabolism work.

The method of collecting twenty-four-hour specimens is, we believe, a new one, and since it has proved to be very satisfactory, should be given in detail. A large number of 20-ounce, round, wide-mouthed bottles with cork stoppers are kept in the ward. These have been etched on the side so that one can write on them with a pencil. At 5 a. m., the time at which the twenty-four-hour period ends, each

COMPOSITION OF FOODS USED IN METABOLISM WARD

Food	Protein	Fat	Carbohydrate	Calories per Gram	100 Calory Portion
Beef, chopped	22.1–48.6	2.4–12.8	0	1.3– 2.0	50– 79
Beef broth	2.1	0.2	0	0.1	1000
Bread, white	9.8	0.3	53.5	2.6	38
Chicken, minced	18.5	7.2	0	1.5– 1.5	69
Cabbage, thrice boiled *	....	....	0.24		
Cauliflower, thrice boiled *	1.75	....	0.12		
Cocoa, powdered	23.1–23.2	19.4–25.2	48.3–54.0	4.8– 5.3	19– 21
Cheese, cottage	14.9–19.2	0.2– 1.9	0	0.6– 0.9	118–164
Crackers, soda	8.3	9.3	73.2	4.3	24
Crackers, sugar	6.2	10.7	80.1	4.5	22
Cream	2.1– 2.9	17.1–19.8	4.0–5.2	1.9–2.1	48– 53
Cream	2.1–2.9	17.1–19.8	4.0–5.2	1.9–2.1	48–53
Custard	5.4	3.5	21.6	1.4	70
Custard, hospital diabetic	5.7	5.7	7.3	1.1	94
Farina, dry	18.9	0.9	68.2	3.7	27
Flour, hospital diabetic	23.2	1.3	68.2	3.9	26
Ice cream, vanilla	3.4– 4.8	1.7– 6.9	12.2–23.4	1.0– 1.6	61– 99
Ice cream, chocolate	3.7	5.5	12.3	1.2	85
Jelly, lemon	2.1	0.2	17.1	0.9	111
Junket	2.1	2.1	16.6	1.0	104
Macaroni, dry	13.7	1.2	77.5	3.9	26
Mammala	26.8	9.6	....	4.2	24
Mammala (separated milk)	31.7	5.4	....	4.0	26
Mammala (full cream)	10.2	28.2	....	5.5	18
Milk, hospital	3.09– 3.1	3.3– 4.67	4.10– 4.7	0.6	166
Oatmeal, dry	15.1	5.6	71.2	4.1	24
Potatoes, mashed	2.2	0.2	18.0	0.9	118
Pudding, rice	4.1	3.0	24.8	1.5	68
Pudding, tapioca	5.7	2.3	14.8	1.1	94
Rice, dry	7.0	0.5	81.9	3.8	27
Rice, cooked	1.4	0.3	13.1	0.6	159
Tapioca	....	....	91.1	3.7	27
Special Articles—					
Cane sugar	Sucrose 100 per cent.			3.96	25.2
Corn sirup—glucose	Glucose, 41.3 per cent.; dextrin, 33.9 per cent.; sucrose, 2.7 per cent.			3.07	32.6
Corn sirup—glucose	Glucose, 42.4 per cent.; dextrin, 44.6 per cent.; sucrose, 0.				
Gelatin					
Lactose	Lactose, 98.4 per cent.			37.0	27.0
Olive oil	....			9.52	10.5
Sherry	Alcohol by volume, 19.45 per cent.; Carbohydrate, 1.96 per cent.			1.46	68.5c.c.
Vinegar	Acetic acid, 4.07 per cent.				
Whisky	Alcohol by volume, 41.76 per cent.			2.96	33.8c.c.

* Cooked in three changes of water.

patient is given a bottle and made to empty his bladder. The bottle is then marked with his name, the date, the hour and minute. The volume is estimated for clinical purposes by comparison with a calibrated bottle of the same capacity. The data are then recorded on a special slip of paper to go to the laboratory and also on the diet chart. A little toluene is added to the urine bottle, which is corked and stored in the ice-box along with the previous voidings of that twenty-four-hour period, each voiding being in a separate bottle. At about 9 o'clock in the morning the laboratory man checks up the bottles with the records on the laboratory slip, and with the nurse's notes takes all the bottles to the laboratory, measures the volume accurately, makes up to volume and analyzes a sample.

The only disadvantage of this system is the labor of carrying a number of half-filled bottles, although this is not great if suitable carriers are used. The advantages are as follows: 1. There is no chance of a specimen of urine having been poured into another patient's bottle thus spoiling two twenty-four-hour specimens. 2. If a single voiding is lost the urine for the remainder of the day can be accurately analyzed. 3. The urine can be fractionated and the nitrogen elimination determined in hourly periods, as is frequently done in calorimeter experiments. 4. The bottles make excellent urinals, are less apt to spill than the ordinary ward urinal and are not unsightly even when filled with urine. 5. Since the urines are made up to volume in the laboratory, it is possible to rinse out each bottle with distilled water and collect every drop of urine. 6. The bottles are washed, dried, and, if necessary, sterilized in the laboratory, so that there is no danger of a patient voiding into a urinal containing decomposing urine. 7. The bottles are cheap and can be kept on hand in large numbers, so that the patients need never wait for the urinal. 8. While we have never had occasion to use them in a general ward, there is no reason why they should not be used instead of the common type of expensive and unsightly urinal. In collecting single specimens for the usual routine analysis the nurse could put a bottle by each bed in the morning and send the desired specimens directly to the ward laboratory without transferring to a special jar. It is surprising how long urines will remain clear if voided into and kept in a clean bottle.

The collection of feces is somewhat more difficult. Patients who can get out of bed defecate into a weighed bucket in the commode. This bucket is then weighed again. A little formalin is added and the whole sent to the laboratory where the specimen is thoroughly mixed and one-tenth removed to be dried and added to the other aliquot portions of that period and analyzed. Bed-ridden patients use a weighed bed pan from which the feces are transferred to a covered bucket for

transportation. Most of the patients with acute diseases are given every morning an enema of hypertonic salt solution. Oil and soap enemas of course interfere with the accuracy of the fat analyses; glycerin enemas make it impossible to dry the feces. To divide the periods, powdered carmin (0.3 gm., 5 grains) is given with the first meal of the period and with the first meal after the period is ended. Experience has shown that it is much easier to determine the exact point of appearance of the carmin in the feces than to find the point of disappearance. When patients are being given enemas it is easier to discover traces of carmin than traces of charcoal. Periods are made as long as possible to minimize the errors of division.

A special diet sheet has been provided by the hospital on which the nurses record the weights of raw material given to the patient and make the calculations from the table of known composition of the food. On this sheet is a summary column giving carbohydrate, fat and protein grams and calories, total calories, nitrogen of the food, of the urine, of the total excreta and the nitrogen balance; weight of the patient and food calories per kilogram. In another place are columns for recording the time and amount of each voiding and each defecation.

Patients are weighed at 9.00 a. m. every day or every other day on a "silk scale" accurate to 10 grams. Bed patients are weighed on a platform resting on these scales in the manner described by Coleman.[3] The nurse slides the patient on the smooth platform which is just at the level of the bed, weighs him and then makes up the bed while he is still on the balance. The whole procedure has been found to be a convenience for the nurse rather than a time-consuming task.

Nitrogen determinations are made by the Kjeldahl method, ammonia, uric acid, creatin, creatinin, and indican by Folin's[4] methods, urea and glucose by the methods of Stanley R. Benedict.[5]

The calorific value of the foods has been determined by means of the Riche[6] bomb calorimeter. Food fat analyses have been made in a Soxhlet apparatus. Carbohydrates were determined by a difference using in the later work a new procedure described by Gephart.[7] The

3. Coleman: Diet in Typhoid Fever: Journal Am. Med. Assn., 1909, liii, 1145.

4. Folin: Approximately Complete Analysis of Thirty Normal Urines, Am. Jour. Physiol., 1905, xiii, 45.

5. Benedict: The Detection and Estimation of Glucose in Urine, Jour. Am. Med. Assn., 1911, lvii, 1193. The Estimation of Urea in Urine, Jour. Biol. Chem., 1910, viii, 405.

6. Riche: An Improved Type of Calorimeter for use with any Calorimetric Bomb, Jour. Am. Chem. Soc., 1913, xxxv, 1747.

7. Gephart, Frank C., and Csonka: In the Estimation of Fat in Feces, Jour. Biol. Chem., 1914, xix, 521.

dried feces were powdered and the fat determined at first by the Kumagawa-Suto method and later by the new saponification procedure described by Gephart.[7] In calculating food values, Rubner's factors were used, namely: for fat 9.3 calories; for carbohydrate and protein, 4.1 calories per gram.

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8. Kumagawa and Suto: Ein neues Verfahren zur quantitativen Bestimmungen des Fettes und der unverseifbaren Substanzen in tierschen Material nebst der Kritik einiger gebrauschlischen Material, Biochem, Ztschr., 1908, viii, 212.

CLINICAL CALORIMETRY

FOURTH PAPER

THE DETERMINATION OF THE BASAL METABOLISM OF NORMAL MEN AND THE EFFECT OF FOOD*

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The importance of the normal control has been emphasized so strongly by the serologists and the management of the control has been developed by them to such an art that it has seemed advisable to apply some of their methods of critique to the study of the respiratory metabolism. Serologists insist that a man shall make his own controls with the same apparatus and exactly the same technic as in the experiments and they also insist that the controls shall be numerous enough to show individual variations in their true proportions. These precautions and many others have been made necessary by the fact that the normal control is usually the point of attack in serological controversies. Likewise in the study of metabolism the normal control is coming to be recognized as the weakest part of the experiment. The chemical methods of blanks and duplicates will not suffice; the living organism is the uncertain factor. The literature is notoriously filled with false theories, of which by far the greater part would never have been promulgated if sufficient attention had been given to normal controls.

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† With the technical assistance of G. F. Soderstrom and R. H. Harries.

The three papers immediately preceding have described the Sage respiration calorimeter in Bellevue Hospital and its adjoining metabolism ward. Before presenting any of the work in pathological conditions it has seemed best to study in detail the results obtained on the normal controls. It was the original intention to use a large number of normal subjects and determine the individual variations in metabolism, but this laborious piece of work was gladly abandoned when it was learned that Benedict and his collaborators were engaged in the task. In pathological conditions the work has been confined as much as possible to men between the ages of 20 and 50 who do not depart very markedly from the normal relationship between height and weight. Consequently the normal controls have been selected to comply with these requirements.

BASAL METABOLISM

As a basis of comparisons between all normal individuals and groups of patients the heat production in the morning from fourteen to eighteen hours after the last meal with the individual at complete rest, was selected. This has been termed the *"nüchtern"* metabolism by the Germans, the "post-absorptive" by Benedict and Cathcart,[1] but the simplest and most satisfactory term is "basal metabolism," a translation of the German *Grundumsatz,* as used by Lusk and his coworkers[2] in the series of papers published under the heading of Animal Calorimetry.

The literature of the respiratory metabolism of healthy men has been admirably reviewed by Benedict and Carpenter[3] in 1910 and Loewy[4] in 1911. In the former monograph the results of a large number of experiments with the respiration calorimeter of Wesleyan University are gathered in numerous tables. During the so-called rest experiments, however, the subjects were allowed to move about the room and indulge in minor muscular activities, something which had

1. Benedict and Cathcart: Muscular Work, Carnegie Institution of Washington, 1913, Pub. 187.

2. Lusk: Calorimetric Observations, Med. Rec., New York, 1912, lxxxii, 925; Williams, Riche and Lusk: Animal Calorimetry, Second Paper. Metabolism of the Dog Following the Ingestion of Meat in Large Quantity, Jour. Biol. Chem., 1912, xii, 349; Lusk: Third Paper, Metabolism After the Ingestion of Dextrose and Fat, Including the Behavior of Water, Urea and Sodium Chlorid Solutions, Ibid., 1912, xiii, 27; Lusk: Fifth Paper, The Influence of the Ingestion of Amino-Acids upon Metabolism, Ibid., 1912, xiii, 155; Lusk: Sixth Paper, The Influence of Mixtures of Foodstuffs Upon Metabolism, Ibid., 1912, xiii, 185.

3. Benedict and Carpenter: The Metabolism and Energy Transformations of Healthy Man During Rest, Carnegie Institution of Washington, 1910, Pub. 126.

4. Loewy: Oppenheimer's Handbuch der Biochemie der Menschen und der Thiere, Jena, 1908, iv,[1] 172.

been permitted in practically all the large respiration chambers. Benedict and Carpenter measured the increased heat production caused by certain simple movements which their subjects had performed during the experiments. The act of rising from a chair, taking one or two steps, opening the food aperture, removing the food, closing the window and returning to the chair required only 19 to 29 seconds, but involved the expenditure of 1.22 calories. Considering the short time involved in the operation, the heat production was increased from 200 to 300 per cent. They also found the metabolism 15 per cent higher when the subject was standing than when he was sitting, and from 8 to 10 per cent. higher when lying awake than when sleeping. The sleeping periods were between 1 a. m. and 7 a. m., and the waking periods followed immediately in the three experiments which were really satisfactory. During the waking periods there was an increase in the oxygen consumption amounting to 1.7, 0.9 and 11.5 per cent., while the heat production was increased 5.8, 15.2 and 13.1 per cent. Some of this increase may be accounted for by difference in the time of day, some by small muscular movements. Johansson[5] found that with complete muscular relaxation the carbon dioxid production was the same as during sleep. The two individuals (H. C. K. and H. R. D.) studied by Benedict and Carpenter produced during sleep 35.2 and 36.2 calories per square meter of body surface, whereas only three of the twelve normal men, whose metabolism is recorded in Table 3, produced more than 35.1 calories per square meter per hour. It is obvious that if the metabolism of H. C. K. and H. R. D. were increased 5.8 per cent., 15.2 per cent. and 13.1 per cent., this increase would carry them just so much farther into the zone where it is necessary to assume muscular activity to account for the abnormally high metabolism.

In anticipation it may be well to mention that the average basal heat production of the individuals we are reporting is 34.7 calories per square meter per hour, the subjects lying awake, at perfect rest during the morning hours. The average heat production of the nineteen subjects of Benedict and Carpenter while asleep between the hours of 1 a. m. and 7 a. m. was 35.3 calories and of fifty-five individuals while awake and moving from time to time in the calorimeter was 49.2 calories per square meter per hour. The fact that their sleeping subjects showed a metabolism 3 per cent. higher than our subjects awake may substantiate the conclusions of Johansson. Benedict and Carpenter pointed out at the conclusion of their monograph (p. 246) the fact that the figure 49.2 calories per square meter per hour, equaling

5. Johansson: Ueber die Tageschwankungen des Stoffwechsels und der Körpertemperatur in nüchternem Zustande und vollsändige Muskelruhe, Skand. Arch. f. Physiol., 1898, viii, 85.

36.5 calories per kilogram per day, represented not the condition of true rest, but rather that of a person confined for the day to a small room but allowed to dress and undress, sit in a chair, feed himself, etc.

Since the appearance of this monograph Benedict and his coworkers, and also other investigators, have insisted more and more strongly on the necessity of absolute quiet in rest experiments and as a check on muscular activity a graphic record of all movements. This eliminates for our purposes practically all the work done in large respiration chambers before 1910 and leaves us only the work done by means of the small types of apparatus, and especially the Zuntz-Geppert apparatus, by Magnus-Levy and Falk,[6] and by Loewy. The results of the determinations on nineteen normal individuals have been collected in a table by Loewy[7] which is reprinted by Benedict and Joslin.[8] Coleman and DuBois,[9] in gathering normal controls to compare with their typhoid patients, grouped these cases of Loewy with twenty-seven normal controls taken from the work of Benedict and Joslin, and with two of their own cases. The average heat production of the total forty-eight normal men was 33.7 calories per square meter of body surface per hour. Very recently Benedict, Emmes, Roth and Smith[10] published a brief report of their important work on the basal metabolism of a total of eighty-nine men and sixty-eight women. The early appearance of these determinations has been of great service to us, and we wish to express our appreciation to these investigators for the publication of the most essential part of their data.* All their determinations were made on healthy subjects in the morning at least twelve hours after the last meal, with the subject at complete rest. Some of the experiments were made in the bed calorimeter of the Nutrition Laboratory of Boston, but most of them were short experiments made with the small Benedict "universal respiration apparatus." The fact that this small machine gives results almost identical with the calorimeter was amply proved by Benedict[8] and his coworkers and confirmed by the limited amount of work done with both types of apparatus by

6. Magnus-Levy and Falk: Der Lungengaswechsel des Menschen in verschiedenen Alterstufen, Arch. f. Anat. u. Physiol., 1899, Supp. 314.

7. Loewy: Oppenheimer's Hand. der Biochemie der Menschen und der Thiere, Jena, 1908, iv,[1] 179.

8. Benedict and Joslin: Metabolism in Diabetes Mellitus, Carnegie Institution of Washington, 1910, Pub. 136; A Study of Metabolism in Severe Diabetes, ibid., 1912, No. 176. Ueber der Stoff- und Energieumsatz bei Diabetes, Deutsch. Arch. f. klin. Med., 1913, cxi, 333.

9. Coleman and DuBois: The Influence of the High Calory Diet on the Respiratory Exchanges in Typhoid Fever, The Archives Int. Med., 1914, xiv, 168.

10. Benedict, Emmes, Roth and Smith: The Basal, Gaseous Metabolism of Normal Men and Women, Jour. Biol. Chem., 1914, xviii, 139.

* A more complete discussion of the work is appearing in the Jour. Biol. Chem., March, 1915.

Coleman and Du Bois.[9] The average heat production of the eighty-nine men was 34.7 calories per square meter per hour, and of the sixty-eight women, 32.2 calories. The lower heat production of women is in accord with the previous findings of Sonden and Tigerstedt.[11]

The work of Magnus-Levy and Falk[6] showing the diminution of metabolism in old age and the increase in youth is also confirmed. The two men over 50 years of age produced only 28.9 calories per square meter. The eight youths between 17 and 20 averaged 37.1 calories, nine who were 20 years old, 36.6 calories, seven who were 21 years old, 36.1 calories.

SPECIFIC DYNAMIC ACTION OF FOODS

The subject of the specific dynamic action of foods in increasing metabolism is fully discussed by Lusk[12] in his text-book and in a series of papers on animal calorimetry.[2, 13]

From his work on dogs, Lusk has concluded that the specific dynamic action of protein is due to the stimulation of the metabolism of the cells by certain of the amino-acids while the action of fat and carbohydrates is due to the mass action of these metabolites in the circulation. He has found marked differences in the action of the various amino-acids and the various carbohydrates. The study of the specific dynamic action of foods on man is not nearly as far advanced as in the case of the dog. Magnus-Levy[14] in connection with his work on dogs found that after giving a man 50 to 60 grams of carbohydrate the metabolism was increased in the first hour from 2 to 12 per cent., in the second hour 0 to 7 per cent. After 140 to 160 grams of starch in bread the increase in the first hour averaged 22 per cent., the second hour 14 per cent., the third hour 16 per cent. After 210 grams of bacon and butter the metabolism was increased 5 to 10 per cent. for seven to eight hours, while after 210 to 250 grams of beef the oxygen consumption rose from 3 to 12 per cent. the first hour and then 15 to 34 per cent. in the next six hours. Gigon[15] obtained similar results using a Jacquet apparatus. In the period of four to five hours following the ingestion of 100 grams of dextrose there was an increase of 9.5 per cent. in the oxygen consumption. After 50 grams of casein the oxygen was increased 5.5 per cent. and after 100 grams 16.8 per cent.

11. Sonden and Tigerstedt: Untersuchungen über die Respiration und den Gesammtestoffwechsel des Menschen, Skand. Arch. f. Physiol., 1895, vi, 99.

12. Lusk: The Science of Nutrition, Philadelphia, 1909, second edition; Stoffwechsel und Ernährung; Deutsche Uebersetzung von L. Hess, 1910.

13. Lusk: The Cause of the Specific Dynamic Action of Protein, The Archives Int. Med., 1913, xxi, 485.

14. Magnus-Levy: Ueber die Grosse des respiratorische Gaswechsels unter dem Einfluss der Nährungsaufnahme, Arch. f. d. ges. Physiol. (Pflüger's), 1894, lv, 1.

15. Gigon: Ueber den Einfluss der Nährungsaufnahme auf den Gaswechsel und Energieumsatz, Arch. f. d. ges. Physiol. (Pflüger's), 1911, cxl, 509.

EXPERIMENTAL PROCEDURE

The normal controls who were kept in the metabolism ward were given a maintenance ration, the last meal of the day being about 5 p. m. At 5 a. m. they were awakened, given an enema, and instead of breakfast, a cup of coffee without cream or sugar. At about half past nine the calorimeter bed was wheeled to the ward on the weighing platform, which is provided with large casters, and the subject lifted from his bed, weighed, rolled back to the calorimeter room and slid into the calorimeter, bed and all. He was dressed in a night shirt, thick ward pajamas and thick socks, and, as a rule, the legs were covered with a sheet, although some subjects needed a thin blanket and others required no covering. A soft pillow was placed under the head and sometimes one under the knees. Every effort was made to ensure absolute comfort, a matter of great importance in work on the respiratory metabolism.

Those normal controls who lived at home took their evening meal at 6 or 7 o'clock, rose at 6 or 7 a. m., drank a cup of black coffee, took the street car, walked about 1/4 mile and arrived at the hospital at 9 o'clock. They then undressed, weighed themselves, dressed in warm pajamas and entered the calorimeter.

As soon as the subject was in the calorimeter the rectal thermometer was inserted about 12 cm. in the rectum, giving slight discomfort for a few minutes, but later remaining in position without the man's being conscious of its presence. The surface thermometers were next fastened tightly to the thorax, axillae or abdomen by means of adhesive plaster and the whole covered with a pad of absorbent cotton about 20 cm. in diameter and 3 or 4 cm. thick, this being held in place by strips of adhesive. The Bowles stethoscope was next strapped over the apex of the heart and the whole covered with night shirt and pajamas. When this was finished the bed was shoved all the way into the box, the ventilation started, and at about a quarter past 10 the glass plates were sealed in the end of the calorimeter and the heavy front put in position, making it possible to start the preliminary period shortly after half past ten.

The actual preparation of the calorimeter had begun long before this. On the previous afternoon all sulphuric bottles, soda-lime containers, etc., had been filled and the oxygen tank weighed so that any leakage over night might be detected. The temperature of the calorimeter room had been watched every hour by the night nurse and maintained within 1 degree of the standard experimental temperature of 23 C. At nine in the morning the water circulation through the various cooling coils and the absorber had been started and a lighted 32 candle power electric lamp placed in the box until the subject was ready. If

these precautions had been carefully followed and if the observer had watched the temperature of the various parts of the apparatus, it was possible to bring the box into perfect equilibrium and control fifteen to twenty minutes after the start of the preliminary period. As we shall see later, there is reason to believe that during the first hour after the box is sealed the wooden frame of the bed may absorb a little heat owing to its proximity to the subject's body.

As a rule the preliminary period lasts thirty to forty minutes and the experiment begins shortly after 11 o'clock. Eight minutes before the start a sign is hung in the window telling the subject to remain absolutely quiet and the first residual sample of ten liters of air is drawn through U tubes by means of the Bohr meter. At four or five minutes before the start the second residual is begun and a tracing of the spirometer curve made in the manner first used by Benedict and Carpenter. At "time" the various cocks and switches are turned

TABLE 1.—The Statistics of the Normal Controls

Subject	Weight, Kg.	Height, Cm.	Chest Circumference, Cm.	Age, Yrs.
G. L.	78.4	175.5	90.5	47
E. F. D. B.	73.6 75.5	178.8	91.5	31-32
F. C. G.	56.5	173.9	80.2	29
R. H. H.	62.0	177.2	85.3	21
L. C. M.	59.5	170.6	86.6	22
Louis M.	51.7	.....	....	22
John L.	70.9	.....	....	44

as described in the previous article. One or two minutes after "time" the subject is allowed to shift his position, and, if necessary, void into a tared urine bottle which he then places on a small spring balance so that the exact weight of urine passed can be read through the calorimeter window. During the remainder of the hour he lies as quiet as possible trying not to turn from back to side and vice versa more than once an hour. The work-adder on the spirometer records each movement and the electrical control of the calorimeter is so delicate that the observer in charge of the thermometers can detect such slight activity as turning the head to look out of the window by the rise in the temperature of the air and wall. At the close of the first and subsequent hours the procedure is the same as at the start, except that only one sample of residual air is analyzed.

The statistics of the normal controls are as shown in the accompanying table (Table 1).

DESCRIPTION OF SUBJECTS AND DETAILS OF EXPERIMENTS

G. L., physiologist, large frame, slightly adipose. Has taken but little exercise during the last few years. Health good, no recent illnesses. Physical examination negative.

Experiment 1.—March 11, 1913. Although this was the first experiment on man made with the Sage calorimeter, the accuracy of the machine had been thoroughly tested by means of the alcohol checks described in Paper 2. The temperature of the air in the calorimeter was 24.5 C. in this experiment instead of the temperature of 23 C. used later. In addition to a suit of pajamas, the subject wore a heavy sweater. The basal metabolism was determined in the first two hours and at the beginning of the third hour he drank a solution of 115 grams commercial glucose (dextrose 42.37 per cent., dextrin 44.57 per cent., water 13.50 per cent.) in 500 c.c. water and 10 c.c. lemon juice. The commercial glucose was equivalent in calories to 100 grams dextrose. The subject, who had felt somewhat too warm during the first two hours, perspired profusely after the glucose. He remained very quiet during the five hours.

E. F. D. B., physician, large frame, moderate adipose. Up to the age of 22 in good athletic condition; since then has exercised in steadily decreasing amounts. During the winter of 1913 took violent exercise for about half an hour twice a week; in 1914 scarcely exercised at all. General health good; no recent illnesses. Heart, lungs, etc., normal.

Experiment 2.—March 13, 1913. The basal metabolism was determined in the first two hours, and at the beginning of the third hour he drank 115 grams commercial glucose in the same solution as in the experiment on G. L. The temperature of the calorimeter was 22 C. and his clothing consisted of thin undershirt and pajamas. He did not perspire but blew his nose several times each hour, spent a good deal of the time looking out of the window and was distinctly more restless than in the subsequent observations.

Experiment 25.—May 17, 1913. Basal determination only. Was very quiet during all three hours and dozed from 11:30 to 11:50.

Experiment 27.—May 22, 1913. At 8:55 a. m., before entering the calorimeter, drank 230 gm. commercial glucose (equivalent to 200 gm. dextrose) in 500 c.c. water and 15 c.c. lemon juice. Six minutes were required to drink the mixture. Dozed at times during the experiment.

Experiment 115.—March 30, 1914. Basal metabolism only. This experiment was conducted by only two observers, Mr. Soderstrom and Mr. Harries, and the periods were made one and one-half hours long to give them more time for weighings, etc. In the subsequent experiments on this subject these two observers alone were able to make all measurements and keep up with the calculations in hourly periods, a record of which they may well be proud, especially since the agreement between the direct and indirect calorimetry was unusually good.

Experiment 116.—April 1, 1914. Just before entering the calorimeter between 9:45 and 10:07 a. m., the subject ate the following meal containing 10.5 gm. nitrogen: fat-free milk, 600; pot cheese (cottage cheese or *Schmierkäse*), 150; egg-white, 120; egg-yolk, 20. During this experiment the work-adder was out of order and recorded part of the excursions of the spirometer due to the admission of oxygen to the box. The subject was very quiet, much more quiet than the work-adder record would indicate.

Experiment 138.—May 8, 1914. Between 10:05 and 10:07 a. m., drank a solution of 200 gm. C. P. Dextrose (Merck) in 400 c.c. water and 35 c.c. lemon juice. No glycosuria resulted in this or any other of the experiments on normal controls.

Experiment 141.—May 15, 1914. An attempt was made to raise the respiratory quotient as high as possible by filling the glycogen stores of the body

before giving the dextrose. At 11:30 the night before the experiment and again at 6:15 in the morning the subject ate the following carbohydate meal: shredded wheat, 55 gm.; milk, 100 c.c.; cane sugar, 10 gm.; in the morning taking an additional 10 gm. cane sugar in coffee. Between 9:50 and 9:53 he drank a solution of 200 gm. C. P. Dextrose in 400 c.c. water and 35 c.c. lemon juice.

F. C. G., chemist, thin. At age of 16 had an attack of malaria lasting two weeks. Has not been sick in bed since then and has never weighed over 64 kg. (140 pounds). Has never taken systematic exercise, except baseball from 1900 to 1906. Appetite fair, sleeps well. Physical examination: complexion pale and somewhat sallow; hemoglobin normal; state of nutrition rather poor; heart, lungs and abdomen normal. Experiment 142, May 18, 1914. Basal determination.

Experiment 3.—March 17, 1913. The basal metabolism was determined between 9:02 and 12:02, the subject going into a profound sleep in the second and third hours. The calorimeter was then opened and the subject ate the *Haferschleim* mixture of Schmidt's test diet. This contained 40 gm. dry oatmeal, 10 butter, 200 milk and one egg, or approximately, protein, 13.1, fat, 10.2, carbohydrate, 35.5 gm. At the end of the observation it was apparent that the respiratory quotients were abnormally low and that the apparent oxygen consumption was much higher than was consistent with the direct calorimetry. The cause for this was found in a leak in the oxygen cylinder, making it necessary to omit the oxygen figures from the data and base the calculations on the direct calorimetry alone.

Experiment 17.—April 22, 1914. Basal determination. The subject remained very quiet, but took care not to go to sleep. Unfortunately the oxygen cylinder leaked again and the calculation of the indirect calorimetry was not accurate.

R. H. H., chemist, tall and spare with long and rather thin bones, very little adipose. At the age of 12 had pneumonia, since then always well. Up to four years ago played semiprofessional baseball or basketball almost every day. Since 1910 his exercise has been limited to four to ten miles of walking a day and in summer a swim of about two miles a day. Physical condition good, heart, lungs and abdomen normal.

Experiment 4.—March 13, 1913. Basal determination. During the experiment this subject tried to void at the beginning of each hour but was unable to do so and was slightly more nervous and more active than the other subjects. He could not void before his first meal after the experiment and it has therefore been necessary to omit the figures for the urinary nitrogen and base the calculations on the tables of Magnus-Levy,[16] assuming that 15 per cent. of the calories were derived from protein.

Louis M., barber, small frame, short and thin, muscles fairly firm. This subject was in the hospital from September 7 to October 30, 1912, with a moderately severe attack of typhoid fever, and served as a subject of numerous observations by means of the Benedict universal respiration apparatus (Coleman and DuBois[9]). He was born in Germany and came to New Orleans in 1911. There he suffered from a severe attack of malaria but has had no recurrences. His family history shows that one sister is insane.

After his attack of typhoid he left the hospital in excellent condition and he has been perfectly well for the last four months, although at first he was somewhat weak and easily tired. Physical examination shows heart, lungs, abdomen, etc., to be normal.

Experiment 7.—March 26, 1913. Basal metabolism. Subject remained in the metabolism ward four days. On the evening previous to this experiment

16. Magnus-Levy: Von Noorden's Handbuch der Pathologie des Stoffwechsels, Ed. 2, 1906.

at 5 p. m., ate a dinner containing protein, 35.1 gm., fat, 37.1, carbohydrate, 105.6. During the experiment he lay very quiet, dozing most of the time.

Experiment 8.—March 28, 1913. March 27 his food contained protein, 80.6; fat, 168.9; carbohydrate, 268.7 gm.; the last meal of the day at 6 p. m. containing protein, 28.9; fat, 61.7; carbohydrate, 82.3 gm. Just before entering the box, between 8:25 and 9:25 a. m., he ate 725 gm. chopped beef, fried in butter, the whole containing 23.93 gm. nitrogen and 100 gm. fat. During the experiment he slept from 12:26 to 1:18 p. m. and from 3:22 to 3:30. There was a small leak from the absorber pipe into the calorimeter, making the apparent water elimination about 1 gram an hour too high.

John L., dentist, medium frame, medium height, well nourished, muscles flabby. This subject, who was born in Sweden, served as a normal control in the metabolism experiments of Dr. R. A. Cooke,[17] who investigated the functional powers of the kidneys. Careful tests showed in this subject a slight delay in the excretion of sodium chlorid, but there were no other signs of kidney disease. He gave a history of moderate indulgence in alcohol. In 1904 he was jaundiced; a few months prior to the experiment he suffered from an infected hand after a dog bite. For the last five years he has been nervous. He was admitted to the hospital Jan. 15, 1914, suffering from a few small boils and a pedicular eruption. His ailments were so slight that he was induced to remain in the hospital as a normal control and, being without a home, he was glad to remain. Physical examination showed a thorax with flaring ribs and an increased anteroposterior diameter of the chest with hyperresonant percussion note and breath sounds somewhat distant. The teeth were in poor condition; blood-pressure, systolic 115 to 130, diastolic 75 to 90.

Experiment 113.—March 26, 1914. Basal metabolism. During the previous day the diet had contained 11.5 gm. KCl and a minimum of NaCl. The last meal at 6 p. m. had consisted of farina, 25; egg-white, 50; yolk, 50; sugar, 50; cream (20 per cent. fat), 60; KCl, 3.5 gm. Blood-pressure March 25, systolic, 140; diastolic, 95; just before the calorimeter experiment, systolic 135, diastolic 105.

L. C. M., laboratory helper, small frame, somewhat short and thin. He was born in Sicily where he lived until the age of 11. Shortly before leaving for this country he suffered from malaria, but since then has been in good health. For the last five years he has worked in the daytime and gone to school at night, consequently has taken but little exercise. Heart, lungs and abdomen normal.

Experiment 136.—May 4, 1914. Basal metabolism.

Experiment 137.—May 6, 1914. Between 9:50 and 9:53 drank a solution of 200 gm. C. P. dextrose in 400 c.c. water and 35 c.c. lemon juice. No glycosuria.

The subjects have been described in detail above and particular attention has been given to the athletic history, since the recent work in Benedict's laboratory (personal communication) has shown a difference in the metabolism of athletes and non-athletic individuals. From a study of the results in previous determinations of the normal metabolism one is led to suspect that a few distinctly abnormal cases have crept in. It has, therefore, been our practice to give the normal controls as careful physical examination as the patients. The importance of this is manifest if one considers that the onset of hyperthyroidism is usually accompanied by the symptoms of exuberant good health.

17. Cooke: Unpublished.

The details of the individual experiments are given below. The body weight at the start of the experiment is determined by weighing the subject shortly before he enters the calorimeter and then making the proper corrections for food, urine and insensible perspiration. All calculations are made from this weight, the surface area being reckoned from Meeh's[18] formula 12.312 $\sqrt[3]{WT^2}$. Some actual determinations of the surface area of E. F. D. B. have shown that Meeh's formula is 14.3 per cent. too high in his case, while it is only 7.3 per cent. too high in the case of R. H. H. Calculated from a new formula, Meeh's figures are 14.5 per cent. too high in the case of G. L., 9.3 per cent. too high in the case F. C. G. and 13.4 per cent. too high in the case of L. C. M. These measurements will be given in detail in a subsequent paper. For purposes of uniformity, however, calculations are based on Meeh's formula, since this has been used in all other metabolism work. The work-adder was not attached to the calorimeter until May 16, 1913, and an exact record of the activity of the subjects was not obtained before this date. After the work-adder as described in Paper 2 was attached it was possible to compare the activity in different periods and in different experiments and express this in terms of the number of centimeters that the plummet was raised by the expansion of air within the box. The excursion of the plummet for certain movements of the subject was roughly calculated as follows: Raising arm to head, 0.3 cm.; lifting telephone to mouth, 4 cm.; turning from back to side, 7 cm.

In the tables the final calculations of calories per hour have been based on the indirect calorimetry as calculated from the oxygen consumption and the respiratory quotient. In the two experiments on F. C. G., where these were inaccurate the direct calorimetry was used, and in one of the hours in the experiment on G. L. where the CO_2 measurement was lost the non-protein R. Q. for the purposes of calculation was assumed to be 1.00.

In the experiments on E. F. D. B. on May 22 there was an evident error in the division of oxygen between the second and third and the fourth and fifth periods, so these were averaged in the final calculations

The methods of calculation have been described in Paper 1, but it may be well to remind the reader that the method of direct calorimetry represents the heat eliminated from the body, plus or minus the heat stored in or lost from the body, when the temperature of the body rises or falls. The calculation of the percentage of calories derived from protein, fat and carbohydrate is based on the urinary nitrogen and the non-protein respiratory quotient.

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18. Meeh: Oberflächenmessungen des menschlichen Körpers, Ztschr. f. Biol., 1879, xv, 425.

Subject Date	Weight Kg.	Period	End of Period	CO_2, Gm.	O_2 Gm.	R. Q.	H_2O, Gm.	Urine N Per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.
G. L. 3/11/13	73.42	Preliminary	A. M. 9:50							
		1st Hr.	10:50	25.26	21.51	0.85	37.03	0.487	72.35	76.77
		2d Hr.	11:50	26.56	25.90	0.75	37.84	0.487	84.85	86.10
		1st Hr. P. C.	P. M. 12:50	29.61	28.57	0.75	37.88	0.404	94.12	87.75
		2d Hr. P. C.	1:50	.....	25.75	....	39.24	0.404	86.76*	92.53
		3d Hr. P. C.	2:50	30.33	23.44	0.94	38.96	0.404	80.86	95.67
E. F. D. B. 3/13/13	73.6	Preliminary	A. M. 9:35							
		1st Hr.	10:35	27.22	25.27	0.78	27.91	0.554	83.52	77.85
		2d Hr.	11:35	25.28	21.32	0.86	26.53	0.554	71.75	71.94
		1st Hr. P. C.	P. M. 12:35	29.51	23.58	0.91	31.19	0.621	80.27	84.87
		2d Hr. P. C.	1:35	31.12	25.50	0.89	30.50	0.621	86.42	82.87
		3d Hr. P. C.	2:35	30.30	24.94	0.88	30.40	0.621	84.41	81.46
		4th Hr. P. C.	3:35	29.92	24.10	0.90	32.02	0.621	81.92	86.02
E. F. D. B. 5/17/13	75.51	Preliminary	A. M. 9:30							
		1st Hr.	10:30	25.41	22.37	0.83	34.22	0.526	74.69	76.83
		2d Hr.	11:30	25.45	21.95	0.84	32.00	0.526	73.60	76.67
		3d Hr.	P. M. 12:30	25.00	21.24	0.86	30.68	0.526	71.41	74.13
E. F. D. B. 5/22/13	76.10	Preliminary	A. M. 9:30							
		2d Hr. P. C.	19:30	31.13	23.04	0.98	36.24	0.581	79.77	84.61
		3d Hr. P. C.	11:30	31.53	25.29	0.97	36.13	0.581	165.80	83.21
		4th Hr. P. C.	P. M. 12:30	32.45	22.49		35.07	0.581		83.91
		5th Hr. P. C.	1:30	31.95	23.84	0.95	36.63	0.581	162.04	84.45
		6th Hr. P. C.	2:30	29.73	18.18		36.78	0.581		84.96
E. F. D. B. 3/30/14	74.34	Preliminary	A. M. 11:25							
		1½ Hrs.	P. M. 12:55	36.10	32.26	0.81	45.08	0.518	107.30	113.13
		1½ Hrs.	2:25	37.53	34.88	0.78	46.48	0.518	115.24	113.14
E. F. D. B. 4/1/14	74.92	Preliminary	A. M. 11:27							
		2d Hr. P. C.	P. M. 12:27	27.47	24.30	0.82	30.51	0.856	80.50	81.65
		3d Hr. P. C.	1:27	29.66	26.17	0.83	31.75	0.830	86.91	81.50
		4th Hr. P. C.	2:27	28.13	25.35	0.81	32.87	0.900	83.60	85.98
		5th Hr. P. C.	3:27	28.83	25.89	0.81	33.39	0.577	86.11	82.75
		6th Hr. P. C.	4:27	27.12	23.86	0.83	32.98	0.577	79.61	83.63
E. F. D. B. 5/8/14	74.75	Preliminary	A. M. 11:05							
		2d Hr. P. C.	P. M. 12:05	30.55	23.41	0.95	32.59	0.604	80.53	76.35
		3d Hr. P. C.	1:05	30.91	24.28	0.93	33.55	0.604	83.08	79.08
		4th Hr. P. C.	2:05	29.37	22.49	0.95	32.48	0.604	77.33	75.63
		5th Hr. P. C.	3:05	30.23	22.06	1.00	32.22	0.604	76.47	76.46
E. F. D. B. 5/15/14	75.02	Preliminary	A. M. 10:50							
		2d Hr. P. C.	11:50	29.60	22.91	0.94	29.06	0.534	78.74	77.76
		3d Hr. P. C.	P. M. 12:50	31.35	22.12	1.03	30.02	0.534	77.26	80.09
		4th Hr. P. C.	1:50	31.07	24.04	0.94	30.73	0.534	82.67	80.23
		5th Hr. P. C.	2:50	29.95	22.21	0.98	30.87	0.534	76.96	79.99
		6th Hr. P. C.	3:50 A. M.	28.46	22.57	0.92	30.46	0.534	77.11	75.02

Direct Calorimetry Cal.	Rectal Temperature, C.	Av. Pulse	Work-Adder, Cm.	Non-Protein R. Q.	Per Cent. Calories from			Calories Per Hour		Remarks
					Prot.	Fat	Carb.	Per Kg.	Per Sq. M.	
	37.26									
78.95	37.30	..	....	0.87	18	37	45	0.92	32.07	Basal.
82.80	37.25	62	....	0.74	15	77	8	1.08	37.61	Basal.
94.21	37.28	88	....	0.75	11	77	12	1.20	41.72	At 11:53 a. m., 115 gm. commercial glucose.
86.54	37.20	..	....	....	12	..	..	1.11*	38.46*	
92.88	37.17	..	....	0.96	13	11	76	1.03	35.84	
	36.88									
78.09	36.90	..	....	0.78	18	62	20	1.13	38.63	Basal.
72.10	36.91	59	....	0.88	20	33	47	0.98	33.19	Basal.
87.12	36.84	57	....	0.94	21	16	63	1.10	37.13	At 11:38 a. m., 115 gm. commercial glucose.
83.46	36.87	64	....	0.91	19	25	56	1.18	39.97	
85.60	36.98	..	....	0.91	19	26	55	1.15	39.04	
84.64	36.99	60	....	0.98	20	19	61	1.11	37.89	
	36.96									
62.89	36.81	57	22	0.83	19	47	34	0.99	33.95	Basal.
77.00	36.80	55	13	0.85	19	41	40	0.97	33.45	Basal.
74.42	36.93	..	10	0.87	19	36	45	0.95	32.46	Basal.
	36.84									At 8:55 a. m., 280 gm. commercial glucose.
72.90	36.75	66	15	1.03	19	0	81	1.05	36.08	
82.51	26.84	63	17	1.02	19	0	81	1.09	37.33	
84.53	36.95	60	14							
82.50	37.01	58	16	0.99	19	2	79	1.07	36.64	
79.32	37.00	60	24							
	36.91									
110.72	36.88	54	30—	0.82	19	51	30	0.96	32.86	Basal.
116.62	36.99	56	37—	0.78	18	62	20	1.03	35.29	Basal.
	36.84									At 9:54 a. m., protein meal (10.5 gm. N).
84.05	36.91	57	24—	0.83	28	42	30	1.07	36.79	
77.92	36.89	57	28—	0.83	25	43	32	1.16	39.72	
86.71	36.93	58	30—	0.81	29	46	25	1.12	38.21	
81.62	36.94	57	26—	0.81	18	53	29	1.15	39.36	
88.88	37.04	58	33—	0.83	19	46	35	1.06	36.39	
	36.66									
75.09	36.67	61	14.1	0.99	20	3	77	1.06	36.36	At 10:05-10:07 a. m., 200 gm. dextrose.
83.22	36.78	61	23.5	0.96	19	11	70	1.11	38.02	
78.61	36.78	61	18.8	0.99	21	2	77	1.03	35.39	
76.05	36.79	62	26.0	1.06	21	..	79	1.02	35.00	
	36.69									
78.83	36.73	55	19.6	0.97	18	8	74	1.05	35.95	At 9:50-9:53 a. m., 200 gm. dextrose.
78.30	36.73	58	22.5	1.09	18	..	82	1.03	35.28	
79.13	36.78	59	33.1	0.97	17	8	75	1.10	37.75	(Carbohydrate breakfast at 6:15 a. m.).
81.32	36.76	59	21.8	1.03	18	..	82	1.03	35.14	
72.36	36.74	57	34.0	0.95	18	15	67	1.03	35.21	

* Estimated from CO_2.

Subject Date	Weight Kg.	Period	End of Period	CO_2, Gm.	O_2 Gm.	R. Q.	H_2O, Gm.	Urine N Per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.
E. F. D. B. 5/18/14	73.70	Preliminary	10:50							
		1st Hr.	11:50	23.92	21.08	0.83	28.08	0.530	70.29	67.48
		2d Hr.	P. M. 12:50	23.85	21.88	0.79	28.08	0.530	72.38	69.37
F. C. G. ... 3/17/13	56.5	Preliminary	A. M. 9:02							
		1st Hr.	10:02	22.80	.....	....	17.77	0.491	.....	54.43
		2d Hr.	11:02	22.92	.....	....	19.69	0.491	.....	59.16
		3d Hr.	P. M. 12:02	22.59	.....	....	20.90	0.491	.....	60.70
F. C. G. ... 3/17/13	56.5	Preliminary	1:00							
		2d Hr. P. C.	2:00	14.86	41.52	0.85	23.05	0.491	139.85	60.85
		3d Hr. P. C.	3:00	28.53	21.08		30.51	0.491		68.89
		4th Hr. P. C.	4:00	22.73	25.27	0.78	26.08	0.491	69.59	62.52
F. C. G. ... 4/22/13	54.82	Preliminary	A. M. 9:45							
		1st Hr.	10:45	21.92	.....	....	25.40	.....	.....	58.96
		2d Hr.	11:45	22.05	.....	....	26.85	.....	.....	61.94
		3d Hr.	P. M. 12:45	21.08	.....	....	26.26	.....	.....	62.60
		4th Hr.	1:45	21.86	.....	....	28.59	.....	.....	63.33
		5th Hr.	2:45	22.08	.....	....	30.09	.....	.....	68.43
R. H. H. ... 3/19/13	62.00	Preliminary	A. M. 9:42							
		1st Hr.	10:42	26.15	21.59	0.88	27.90	.....	73.54	66.50
		2d Hr.	11:42	27.42	20.98	0.95	28.93	.....	72.78	69.27
Louis M. ... 3/26/13	51.70	Preliminary	A. M. 10:10							
		1st Hr.	11:10	20.53	18.73	0.80	28.92	0.522	61.91	64.64
		2d Hr.	P. M. 12:10	19.95	17.40	0.83	26.95	0.522	57.99	64.44
		3d Hr.	1:10	22.44	20.07	0.81	28.10	0.522	66.57	71.00
		4th Hr.	2:10	18.34	18.05	0.74	25.73	0.522	58.71	66.51
		5th Hr.	3:10	22.18	20.71	0.78	27.36	0.522	68.20	68.88
		6th Hr.	4:10	19.36	19.23	0.73	25.85	0.522	62.51	67.86
Louis M. ... 3/28/13	53.49	Preliminary	A. M. 11:14							
		3d Hr. P. C.	P. M. 12:14	23.43	22.62	0.75	24.08	0.708	73.76	64.89
		4th Hr. P. C.	1:14	24.27	22.67	0.78	29.15	0.695	74.44	75.48
		5th Hr. P. C.	2:14	26.84	25.11	0.78	34.80	0.970	82.02	79.07
		6th Hr. P. C.	3:14	26.44	25.11	0.77	34.38	1.014	81.70	77.18
		7th Hr. P. C.	4:14	24.85	23.21	0.78	35.42	1.188	75.88	83.35
		8th Hr. P. C.	5:14	26.25	24.79	0.77	34.71	1.112	80.53	81.28
John L. 3/26/14	70.94	Preliminary	A. M. 11:20							
		1st Hr.	P. M. 12:20	21.12	19,51	0.79	25.77	0.363	64.65	66.00
		2d Hr.	1:20	21.37	19.62	0.79	24.56	0.363	65.10	68.26
		3d Hr.	2:20	21.07	19.97	0.77	24.01	0.363	65.85	66.72
L. C. M. .. 5/4/14	59.50	Preliminary	A. M. 11:02							
		1st Hr.	P. M. 12:02	22.39	20.71	0.79	28.32	0.534	68.34	71.73
		2d Hr.	1:02	22.14	18.98	0.85	27.28	0.534	63.57	70.36
L. O. M. .. 5/6/14	60.98	Preliminary	A. M. 10:52							
		2d Hr. P. C.	11:52	29.94	23.73	0.92	33.43	0.578	81.05	73.19
		3d Hr. P. C.	P. M. 12:52	30.30	22.08	1.00	32.38	0.578	76.45	74.95
		4th Hr. P. C.	1:52	30.65	21.90	1.02	32.94	0.578	76.21	77.37

—(Continued)

Direct Calorimetry Cal.	Rectal Temperature, C.	Av. Pulse	Work-Adder, Om.	Non-Protein R. Q.	Per Cent. Calories from			Calories Per Hour		Remarks
					Prot.	Fat	Carb.	Per Kg.	Per Sq. M.	
	36.76									
67.14	36.76	57	9.8	0.83	20	46	34	0.96	32.48	Basal.
70.23	36.78	57	18.2	0.79	19	58	23	0.98	33.45	
	37.03									
58.83	37.15	..	....	....	..	..	..	1.04	30.75	Basal. Profound sleep during second and third periods. O_2 leak.
55.75	37.11	..	....	....	..	..	..	0.99	32.45	
56.99	37.06	..	....	....	..	..	..	1.01	31.43	
	37.02									
66.85	37.17	..	....	0.86	19	39	42	1.18	36.87	At 12 m., plate of oatmeal. O_2 leak.
60.53	37.00	..	....					1.07	33.39	
60.83	36.95	..	....	0.78	19	61	20	1.06	33.59	
	37.04									
57.28	37.03	74	....	....	..	..	..	1.04	32.22	Basal. O_2 leak.
62.68	37.07	68	....	....	..	..	..	1.14	35.25	
60.60	37.04	64	....	....	..	..	..	1.10	34.08	
58.15	36.94	66	....	....	..	..	..	1.06	32.71	
64.88	36.87	70	....	....	..	..	..	1.18	36.49	
	36.76									
69.22	36.82	..	....	....	..	..	..	1.19	38.12	Basal. Urine not obtained.
70.31	36.85	..	....	....	..	..	..	1.19	37.78	
	37.18									
58.39	37.07	..	....	0.80	22	56	24	1.20	36.23	Basal.
61.88	37.04	..	....	0.84	24	40	36	1.12	33.92	
75.26	37.15	..	....	0.82	21	49	30	1.29	38.95	
59.27	37.00	..	....	0.72	24	73	3	1.14	34.35	
70.95	37.08	..	....	0.77	20	63	17	1.32	39.91	
62.47	36.98	..	....	0.71	22	77	1	1.21	36.58	
	37.10									
74.89	37.28	..	....	0.74	25	68	7	1.39	42.20	8:25-9:25 a. m., 725 gm. chopped beef = 23.98 gm. N + 100 gm. fat.
81.49	37.43	..	....	0.77	25	59	16	1.40	42.59	
74.67	37.36	..	....	0.76	31	55	14	1.54	46.92	
78.43	37.41	..	....	0.75	33	58	9	1.54	46.74	
80.09	37.38	..	....	0.76	40	49	11	1.42	43.12	
81.96	37.39	..	....	0.75	37	54	9	1.51	46.07	
	37.11									
52.70	36.89	61	13.0+	0.78	15	62	23	0.91	30.64	Basal.
68.56	36.94	55	13.0+	0.79	15	61	24	0.92	30.85	
62.04	36.88	57	33.7	0.76	15	69	16	0.92	31.21	
	36.94									
66.95	36.85	74	22.0+	0.78	21	59	20	1.15	36.41	Basal.
73.48	36.92	70	18.2	0.86	22	37	41	1.07	33.87	
	36.84									
65.74	36.70	85	19.1	0.95	19	15	66	1.33	42.48	9:50-9:53 a. m., dextrose, 200 gm.
73.60	36.68	82	30.1	1.06	20	..	80	1.25	40.07	
82.50	36.79	79	38.2	1.08	20	..	80	1.25	39.94	

The results are expressed in terms of grams and calories per hour, since this is the length of period used in the Cornell and Sage calorimeters and is the nearest unit of the length of the actual experimental period used in most of the modern machines.

DISCUSSION OF RESULTS

As explained in Paper 1 of this series, the determination of the heat production by the methods of direct and indirect calorimetry have been found to give identical results in the work of Rubner, Atwater and Benedict, Lusk and his coworkers. Rubner demonstrated this on the dog in long periods, Atwater and Benedict on man at rest and at work, Lusk on dogs in hourly periods and Howland, in Lusk's laboratory, on babies both normal and atrophic. To this list may be added the work of Armsby[19] on cattle in twenty-four-hour experiments and the work of Carpenter and Murlin[20] who studied the metabolism of women before and after confinement, in Benedict's laboratory. A comparison of the figures for direct and indirect calorimetry obtained in Benedict's calorimeter shows excellent agreement in the two- and three-hour periods. Out of a total of twenty-eight periods, the two methods were within 5 per cent. of each other in seventeen, while only six showed a disagreement over 10 per cent.

Table 3 gives in parallel columns the calories in each of our experiments as measured by the methods of direct and indirect calorimetry. The totals of all the experiments show that the two methods come within 0.17 per cent. of each other. Even when we consider periods as short as one hour, the agreement may be striking. On the normal control, E. F. D. B., there were a total of 26 one-hour periods. In 17 of these the methods of direct and indirect calorimetry agreed within 5 per cent., in 6 periods within 6 to 9 per cent., while three isolated periods showed a disagreement of 11, 12 and 16 per cent., respectively. Work with the Sage calorimeter on normal controls and on patients with a large variety of diseases has shown that in a total measurement of 27,632 calories the direct calorimetry gives a figure only 1.62 per cent. lower than the indirect. There is, therefore, no reason to believe that in long periods, or in the average of a number of short periods, there is any essential difference between the two methods. As will be shown later, there is good reason to believe that indirect calorimetry gives the more accurate results in short periods.

There are two methods of calculating the indirect calorimetry, both of which involve factors that change with the respiratory quotient.

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19. Armsby: Food as Body Fuel, Pennsylvania State College Agricultural Experiment Station, Bull. 126.

20. Carpenter and Murlin: The Energy Metabolism of Mother and Child Just Before and Just After Birth, The Archives Int. Med., 1911, vii, 184.

TABLE 3.—SUMMARY OF RESULTS. AVERAGES OF PERIODS

Subject	Date	Weight at Start, Kg.	Square Meters Body Surface (Meeh)	Calories per Sq. M. per Hour	Variation from Average Normal Basal 34.7	Per Cent. Rise above Subject's Own Basal Metabolism	Average R. Q.	Total Calories Measured in Each Experiment: Method of Indirect Calorimetry	Total Calories Measured in Each Experiment: Method of Direct Calorimetry Rectal Temp.	Method of Direct Calorimetry Surface Temperature	Character of Experiment
G. L.	3/11/13	78.42	2.256	34.84	+ 0	..	0.80	157.40	161.75	......	Two basal hours.
	3/11/13	78.42	2.256	38.67	....	11	....	261.54	273.63	......	First three hours after 115 Comm. glucose = 100 C. P. dextrose
E. F. D. B. .	3/13/13	73.6	2.162	35.91	+ 3	..	0.82	155.27	149.79	......	Two basal hours.
	3/13/13	73.6	2.162	38.51	....	7	0.90	333.02	341.22	......	First three hours after 115 Comm. glucose = 100 C. P. dextrose
	5/17/13	75.51	2.200	33.29	— 4	..	0.84	219.70	214.31	......	Three basal hours.
	5/22/13	76.10	2.211	36.82	....	11	0.97	407.11	401.96	......	1½ to 5½ hours after 230 Comm. glucose = 200 C. P. dextrose.
	3/30/13	74.34	2.177	34.08	— 2	..	0.80	222.50	227.34	232.23	Three basal hours.
	4/ 1/13	74.92	2.188	38.09	....	12	0.82	416.75	419.18	413.58	1½ to 6½ hours after protein meal (10.5 gm. N).
	5/ 8/13	74.75	2.185	36.32	....	10	0.96	317.41	307.97	317.60	1 to 5 hours after 200 C. P. dextrose.
	5/15/13	75.02	2.190	35.87	....	9	0.96	392.74	389.94	395.82	1 to 6 hours after 200 C. P. dextrose taken 3½ hours after breakfast
	5/18/13	73.70	2.164	32.97	— 5	..	0.81	142.67	137.87	138.33	Two basal hours.
F. C. G. ..	3/17/13	56.5	1.813	31.54	— 9	..	....	*	......	......	Three basal hours..
	3/17/13	56.5	1.813	34.60	....	10	....	*	......	......	1 to 4 hours after breakfast of protein 13.1, fat 10.2, carbohydrate 35.5
	4/22/13	54.82	1.778	34.15	— 2	....	....	146.32	139.53	......	Five hours basal.
R. H. H. ..	3/19/13	62.00	1.929	37.93	+ 9	..	0.92	146.32	139.53	......	Two hours basal.
Louis M. ..	3/26/13	51.70	1.709	36.66	+ 6	..	0.78	375.89	398.22	......	Six hours basal.
	3/28/13	53.49	1.748	44.61	....	22	0.77	467.88	471.53	......	2 to 8 hours after 725 gm. beef = 23.93 N and 100 fat
John L. ..	3/26/14	70.94	2.110	30.90	—11	..	0.78	195.60	188.30	188.50	Three hours basal.
L. C. M. ..	5/ 4/14	59.50	1.887	35.14	+ 1	..	0.82	131.91	140.48	141.73	Two hours basal..
	5/ 6/14	60.98	1.908	40.88	....	16	0.96	238.71	221.98	225.28	1 to 4 hours after 200 gm. C. P. dextrose.
Total								4577.37	4569.40		......

* Oxygen figures discarded on account of leaks.

The first is the standard method of Zuntz and his associates, based on the liters of oxygen consumed, which are multiplied by a factor that increases about 8 per cent. as the quotient rises from 0.72 to 0.97. The second method is based on the liters of CO_2 produced, the figure for which is multiplied by a factor which decreases 24 per cent. as the

TABLE 4.—Heat Production of Normal Men, Ages 20 to 50. Comparison of Calories per Kilogram and per Square Meter

Subject	Weight, Kg.	Calories per Kilogram per Hour	Calories per Sq. Meter per Hour	Percentage Variation from Average		Calories per Sq. Meter per Hour According to New Surface Area Formula	Per Cent. Variation from Average
				Calories per Kg.	Calories per Sq. Meter		
F. G. B.*	83.0	1.01	35.8	− 4	+ 5	....	...
G. L.	78.4	1.00	34.8	− 5	+ 2	40.7	+2
F. A. R.*	74.3	0.95	32.4	− 9	− 5	....	...
E. F. D. B.	74.3	1.00	34.1	− 5	0	39.8	−0
John L.	70.9	0.92	30.9	−12	−10	....	...
J. J. C.*	67.6	0.96	31.7	− 8	− 7	....	...
J. R.*	66.0	1.00	32.8	− 5	− 4	....	...
R. H. H.	62.0	1.18	37.9	+14	+11	40.9	+3
L. C. M.	59.5	1.11	35.1	+ 6	+ 3	40.5	+2
F. C. G.	54.8	1.10	34.2	+ 5	0	37.7	−5
Louis M.	51.7	1.21	36.7	+16	+ 7	....	...
T. M. C.*	49.0	1.13	33.8	+ 8	− 1	....	...
Average	....	1.05	34.2	± 8.1	± 4.6	39.9	±2.4
79 normal men in groups† 8 weights	75-85	1.01	35.2	− 7	+ 2	....	...
20 weights	65-75	1.02	34.1	− 6	− 2	....	...
41 weights	55-65	1.09	34.7	+ 1	0	....	...
10 weights	45-55	1.18	35.5	+ 9	+ 2	....	...
Average	.....	1.08	34.7	± 5.8	± 1.5	....	...

* Determinations made by Benedict and Joslin.[29]
† Taken largely from work of Benedict, Emmes, Roth and Smith.[10]

quotient rises from 0.72 to 0.97. Tables for this latter calculation are given by Benedict and Talbot,[21] who prefer this method in using an apparatus in which they consider that for short periods the determination of the carbon dioxid is more exact than the determination of

21. Benedict and Talbot: Studies in the Respiratory Exchange of Infants, Am. Jour. Dis. Child., 1914, viii, 1; The Gaseous Metabolism of Infants, Carnegie Institution of Washington, Pub. 201.

oxygen. It is true that in the closed circuit type of apparatus the measurement of the oxygen is subject to many corrections for changes in the barometer, temperature, moisture, etc., and that it is liable to a plus error in the case of leaks. This error affects the quotient and produces such a change in the CO_2 factor that one usually obtains better results by basing the calculations on the oxygen. This is brought out clearly in Table 5, which gives a comparison of the methods of calculating the heat production from the oxygen and from the CO_2, showing the errors in the results arising from various assumed errors in the measurements. It will be noted that in the great majority of the cases

TABLE 5.—Comparison of Methods of Calculation with Assumed Errors in Measurement of CO_2 and O_2

CO_2		O_2		R.Q.	Calorific Value 1 Liter of CO_2		Calorific Value 1 Liter of O_2		Indirect Calorimetry Based on CO_2		Indirect Calorimetry Based on O_2	
Liters	Assumed Error %	Liters	Assumed Error %		Cal.	Per Cent. Change	Cal.	Per Cent. Change	Cal.	Per Cent. Error	Cal.	Per Cent. Error
12.94	0	15.64	0	0.83	5.829	.....	4.807	.....	75.40	.....	75.17	.....
12.94	0	17.20	+10	0.75	6.319	+8.4	4.708	−2.1	81.74	+8.4	80.98	+7.7
14.23	+10	15.64	0	0.91	5.424	−7.0	4.904	+2.0	77.18	+2.4	76.70	+2.0
12.94	0	16.42	+5	0.79	6.062	+4.0	4.758	−1.1	78.44	+4.0	78.13	+3.9
13.59	+5	15.64	0	0.87	5.617	−3.6	4.855	+1.0	76.33	+1.2	75.93	+1.0
12.29	−5	16.42	+5	0.75	6.319	+8.4	4.708	−2.1	77.66	+3.0	77.31	+2.8
13.59	+5	14.86	−5	0.91	5.424	−7.0	4.904	+2.0	73.71	−2.2	72.87	−3.1
12.94	0	14.86	−5	0.87	5.617	−3.7	4.855	+1.0	72.68	−3.6	72.15	−4.0

cited the error from the use of the oxygen factor is smaller than that from the CO_2. Even with a plus error of 5 to 10 per cent. in the oxygen and no error in the CO_2, the results obtained by using the oxygen are the better, since the minus change in this factor compensates for part of the error. In the two instances shown, in which the results obtained by the use of the CO_2 factor are closer to the theory than those obtained by the use of the oxygen factor, it will be noted that there is a minus error in the oxygen. This is the least frequent of all the errors.

Many investigators in seeking for an index of the heat production express the results in grams or cubic centimeters of CO_2, and compare the elimination of this gas in different individuals, apparently with the impression that they are comparing the actual total metabolism. As we have seen above, a man eliminating, say, 3.13 c.c. CO_2 per kg. per min-

ute might have a heat production 24 per cent. higher than another man eliminating the same amount of CO_2 whose respiratory quotient was at the other end of the scale. If one uses the oxygen consumption the possible error from this source is diminished to 8 per cent. Since it is such an easy calculation to determine the actual calories by using the oxygen figure and the respiratory quotient, it seems inexcusable to leave the results at a stage which might give false impressions. It is only in special investigations on the ventilation of the lungs, etc., that the amounts of the gases themselves are of any direct interest. In most experiments it is the actual calories that need to be determined.

Experience has shown that with careful technic the indirect calorimetry in hourly periods remains fairly uniform in fasting experiments and shows regular curves in experiments after food. The direct calorimetry in hourly periods is a matter of greater technical difficulty on account of the fact that the human body is poorly constructed for accurate thermal measurements. As was shown in Paper 1, a rise or fall of 1 degree centigrade in the average temperature of the body means a storage or loss of about 58 calories if the man weighs 70 kilograms. This is based on the assumption that the specific heat of the body is 0.83, a figure which has been accepted for many decades, although without satisfactory experimental support. Rubner[22] has found that the specific heat of lean flesh is 0.828, of fatty tissue 0.53 and of pure fat 0.45. Rosenthal[23] at an earlier date had made the following determinations: compact bone 0.30, spongy bone 0.710, defibrinated blood 0.927, dried muscle 0.330. Using these figures and the figures for the average composition of the body as given by Vierort[24] one obtains a specific heat of approximately 0.77. A body rich in fat would, of course, approach the figure 0.45 and one rich in water would approach 1.00. Theoretically, one should change the specific heat each time a subject drinks water or voids. This latter would be a matter of small importance, but in the case of a very obese person one-half of whose weight consisted of fat, the true specific heat would not be far from 0.64.

In normal subjects the temperature changes in hourly periods are small and according to the work of Benedict and Slack,[25] the temper-

22. Rubner: Kalorimetrie, Tigerstedt's Handbuch der physiologische Methoden, i, 170.

23. Rosenthal: Ueber die specifische Wärme thierische Gewebe, Arch. f. Physiol., 1878, p. 215.

24. Vierort: Daten und Tabellen. Jena, 1893, p. 249.

25. Benedict and Slack: A Comparative Study of the Temperature Fluctuation in Different Parts of the Human Body. Carnegie Institution of Washington, 1911, Pub. 155.

ature curves in different parts of the body are nearly parallel. Lusk[26] and his coworkers did not find this to be the case in the dog after the ingestion of large amounts of food since this caused a greater rise in surface than in rectal temperature. When one considers the mechanism of the regulation of body temperature in fever it becomes evident that the rise in surface temperature follows that of the internal temperature. Every clinician has felt in some patients, particularly those seriously ill, the extremities growing colder and colder while the internal temperature is rising and, conversely, has felt the surface grow warmer while the temperature is falling, demonstrating the fact that the two are not always parallel.

It was on account of these considerations that the surface thermometers described in Paper 2 were used after May, 1913, the two units of the surface thermometer being strapped over the right and left pectoralis major as near as possible to the heart and dome of the liver. They were covered with a thick layer of cotton in an effort to obtain the temperature of the subcutaneous tissue rather than that of the naked skin. After March 12, 1914, a second surface thermometer was added and its two units placed in various parts of the anterior surface of the thorax and abdomen and also in the axillae. The results have been confusing and difficult to interpret, but they have indicated clearly that the different parts of the body do not show parallel temperature curves. A fruitless search has been made for some part of the body which will give a true index of the mean temperature change. In the majority of all the experiments the rectal temperature was the more satisfactory, but in typhoid fever the surface gave better results. The method of investigation was as follows:

In a total of eighty-five experiments satisfactory rectal and surface temperature measurements were made. Twenty-eight of these experiments were on typhoid fever patients. For the reasons above stated the heat production as determined by the method of indirect calorimetry was considered to be the true heat production, and the results of the direct calorimetry as calculated by three different methods were compared with this as shown in the table below. In all three methods the figure for the heat eliminated from the body was, of course, the same. To obtain the heat produced, the heat stored in or lost from the body, as determined by each of the two measurements, and by a mean of the two, has been added to or subtracted from the heat eliminated.

It will be seen from Table 6 that in the total of 85 experiments the rectal temperature gave the best results, approximating the theoretical more closely than either of its competitors in 36 cases, coming within 5

26. Williams, Riche and Lusk: Metabolism of the Dog Following the Ingestion of Meat in Large Quantity, Jour. Biol. Chem., 1912, xii, 349.

per cent. in 62 cases and involving a total error of only 0.90 per cent. While the surface temperature gave the best results in 24 cases, it showed an error of over 15 per cent. in 5 cases and did not prove as reliable as the mean of surface and rectal. In typhoid fever the honors were more evently divided and all three methods gave surprisingly good results in spite of the large changes in body temperature sometimes encountered. The surface temperature alone gave the best results in 13 of the 28 experiments and also the lowest total error.

TABLE 6.—Comparison of Surface and Rectal Temperatures as an Index of Average Body Temperature; Percentage Differences between Indirect Calorimetry and Direct Calorimetry Calculated According to Three Methods

Percentage Difference in Individual Experiments	Number of Experiments Falling in Each Group					
	Twenty-Eight Typhoid Experiments			Eighty-Five Experiments in Various Diseases, Including the Twenty-Eight Typhoid Observations		
	Rectal Temperature Alone	Surface Temperature Alone	One-half Rectal, One-half Surface	Rectal Temperature Alone	Surface Temperature Alone	One-half Rectal, One-half Surface
0 to 5	18	18	18	62	41	53
5 to 10	9	9	10	19	28	27
10 to 15	1	1	0	4	11	4
15+	0	0	0	0	5	1
Total difference	−1.82	−1.17	−1.24	−0.90	−1.46	−1.18
Number giving results nearest to indirect	8	13	7	46	24	15

As a result of the above analysis the rectal temperature has been adopted as the standard indicator of the average body change in hourly periods, but with a full realization of its limitations. In many experiments, particularly in those with rapidly changing temperature, better results would be obtained by using the surface temperature, but surface thermometers are more easily displaced than rectal and are not so reliable in the long run. Theoretically, one would obtain the best results by the use of many thermometers placed in the rectum, axillae, groin, on the surface of the body in many areas, giving each measurement an estimated weight, and then calculating the mean temperature change. Our attempt to do this in a small way by giving the rectal and surface equal weights did not lead to better results. For many reasons it seems advisable to attach as little apparatus as possible to the subject, and it is

doubtful if the use of many thermometers at one time will ever become a standard method.

There may be several reasons why these results are not in accord with the conclusion of Benedict and Slack. Working with normal subjects who showed comparatively small fluctuations in body temperature, they made many measurements at different depths in the rectum and vagina and found that while there was a sharp fall in temperature between a point 7 cm. within the rectum and a point just within the anus, nevertheless the temperature of points at different depths remained parallel, though at a different level. Temperatures taken in the well-closed axilla and groin were also parallel with the rectal. The mouth was found to be an unsatisfactory place to obtain the mean body temperature. Considerable difficulty was experienced in obtaining satisfactory measurements of the surface of the body and of the hands, and the writers speak of the difficulty of devising a thermometer that will be shielded so that it may assume the body temperature and yet not interfere with the natural liberation of heat.

As we have mentioned above, our surface thermometers were covered with a thick layer of cotton wool and represented a subcutaneous rather than a surface measurement, and therefore not comparable to the axillary, groin and shallow rectal measurements of Benedict and Slack. All of the latter are in the neighborhood of large blood-vessels and might be expected to rise and fall simultaneously.

All of this brings us back to the desirability of using the method of indirect calorimetry as the standard and checking its accuracy by the level of the respiratory quotient and the agreement with the direct calorimetry. All the evidence of this laboratory shows that the quotient rises and falls in regular curves in rest experiments when hourly periods are used. If, therefore, in any experiment the quotient shows a variation not accounted for by recent food, we suspect an error and usually find it compensated for in the next period. This error is almost always found in the calculation of the residual oxygen in the box at the close of the hour. Luckily there is an automatic correction in the method of calculating the indirect calorimetry. If in the first hour the oxygen estimation be too high, the quotient will be too low, and consequently the factor by which the oxygen is multiplied will be diminished. In the second hour when the error has been compensated for, the oxygen estimation will be too low, the quotient too high and the factor increased. This is another reason why the indirect calorimetry is more reliable than the oxygen consumption as an index of metabolism.

The method of direct calorimetry serves as an invaluable check, and if in any two- or three-hour experiment during which the body

temperature changes less than half a degree, the methods of indirect and direct calorimetry do not agree within 5 per cent., one should suspect a defect in the calorimeter. If in the next experiment a similar divergence be found, an alcohol check should be made and the error located. If one can prove that the error was due to any one particular determination, all calculations affected by this must be rejected as in the two experiments on F. C. G. It is by no means necessary to reject the results of the method of calorimetry not affected by the error. There is only one determination that enters into both methods of calculation, but an error in this would cause the two methods to diverge and not to err in the same direction. If through gross carelessness the first sulphuric acid bottle were allowed to gain so much weight that water vapor passed by into the CO_2 absorber, the direct calorimetry would be too low and the indirect too high, since both the quotient and the oxygen factor would be increased.

DETERMINATION OF THE AVERAGE NORMAL

The selection of the proper normal base line is a matter of extreme difficulty. It is also a matter of prime importance in determining whether or not a patient or group of patients shows a total metabolism which is above or below the normal limits. In dealing with patients suffering from acute diseases it is sometimes possible to wait until the patient recovers completely and then determine his normal heat production. This is not always practicable and even when it can be done one has no guarantee that the metabolism has returned to normal unless several measurements at considerable intervals be made. In the case of patients with chronic diseases this method is out of the question. The method most commonly used is that of selecting groups of normal controls to correspond as nearly as possible to each individual patient. This of course is the ideal method if many controls be selected, but it is extremely doubtful if any investigator up to the present date has been able to gather enough satisfactory controls for each patient. The recent work of Benedict, Emmes, Roth and Smith[10] may remedy this, on account of the large number of individuals whose metabolism was determined. Even with this wealth of material one may err if allowed to pick out a small group. The individual variation is large, as one can see from a careful study of the figures. It is, perhaps, unfair to draw many deductions before the full description of the subjects is published, but we may rely on the statement that all were in presumably good health. The average heat production of the 89 men was 833 calories per square meter per day or 34.7 calories per square meter per hour. The average heat production of the 12 men studied in the bed calorimeters and grouped in Table 4 was 34.2 calories

per square meter per hour. This striking agreement is another proof that the Benedict universal respiration apparatus gives results which are almost identical with the calorimeter. For this reason the 7 subjects examined by us have for purposes of calculation been grouped with the 89 of Benedict, Emmes, Roth and Smith. In order to rule out those who were distinctly over- or underweight, the subjects were all plotted in a curve, the height forming the abscissa and the weight the ordinates. All but 9 of the subjects could be grouped between two lines not very far apart. Of the 9, W. S., O. F. M., Prof. C., H. F., F. E. M. and F. A. R. were evidently much heavier in proportion to their height than their fellows, and for this reason excluded from the averages. It is interesting to note that their average heat production was 31.5 calories per square meter. Two of the 9, R. A. C. and B. N. C., were evidently very light in proportion to their height. E. P. C. came just outside the line, but so close to it that he has not been excluded from the averages. All those over 50 years of age were arbitrarily excluded and also those under 20 years. To the remaining 72 were added the normal controls of the present paper. This process of exclusion and addition left a fairly homogeneous total of 79 whose average metabolism was 34.7 calories per square meter per hour, or exactly the same as that of the original 89 before the addition of 7 and the exclusion of 17. These 79 have been divided into four groups according to body weight in Table 4.

If we plot the heat production of all the subjects according to surface area, the range of individual variation becomes apparent. Of the total 79 we find 40 within 5 per cent. of the base line drawn at the average figure 34.7, 28 are from 5 to 10 per cent. from the average and 11 are more than 10 per cent. from the average. Of these, 6 were between 10 and 14 per cent. above, and 5 were between 10 and 15 per cent. below. This means that when we speak of a normal average we must remember a normal variation of at least 10 per cent. above and below and realize that in about 14 per cent. of the normal men the variation may be plus or minus 10 to 15 per cent. One cannot help but feel that most of the cases showing a variation of more than 10 per cent. from the average will be found to present some distinct cause for the unusual metabolism, such as an unusual degree of muscular development or muscular disuse or an unsuspected disturbance of the thyroid secretion, or the mild infection with tuberculosis which all of us pass through at some time in our lives. At any rate, one can be fairly certain that if the total heat production be 15 per cent. from the average it is distinctly abnormal, and if it be more than 10 per cent. from the average it must be regarded with great suspicion.

It may be argued that some of the variation may be due to differences in body weight. If we study the 24 normal subjects in the table we have been considering, whose weights are between 60 and 65 kg., the same variation is apparent. Of the 24, only 13 are within 5 per cent. of the average, 5 are between 5 and 12 per cent. above and 6 are from 5 to 10 per cent. below. If one investigator chanced to select this last group of 6 for his controls his average would be about 15 per cent. lower than if he selected the group of 5 cases with high metabolism. This of course is an extreme instance. It may still be argued that the factor of height must be considered. In the same table we find an exceedingly homogeneous group of 7 men whose weights are between 60.1 and 60.5 kg. and whose heights are between 171 and 175 cm. Even in this group there is a difference of 13 per cent. between the highest and the lowest and a difference of 9 per cent. between the averages of the highest 4 and the lowest 3 in this group.

This somewhat lengthy discussion is intended to show the chances of serious error in selecting any small group of normal controls to compare with a pathological case. One cannot say just how large the group should be, but it is safe to say that it must exceed 5, should exceed 10 and if possible, 50. It is obviously much better to use all the normal controls so far studied and let personal selection play no part. This can be done by basing all comparisons on the average heat production per square meter of body surface.

In Table 4 we find a comparison of the heat production calculated according to surface area and according to weight. A study of the percentage variation from the average shows clearly that all four weight groups are within 2 per cent. of the mean heat production per square meter of body surface. In other words, one can determine the average normal by this method by using a group of individuals of any weight within ordinary limits. On the other hand, the figures per kilogram of body weight show the customary diminution as weight increases and there is a difference of 16 per cent. between the heavy group and the light group. In other words, there is no such thing as an average calories per kilogram for normal men, but only a normal average for each weight. To find the normal for a given man by this method one must consult a curve. To find the normal for a given man by the method of surface area one needs only to remember the figure 34.7.

Shortly after the experimental work on the normal controls was completed it seemed advisable to investigate the accuracy of Meeh's formula and if possible devise a new formula which could be applied to individuals who depart materially from the average body form. Five subjects were measured and it was found that there was a con-

sistent plus error in Meeh's formula which, in the case of a very fat woman, amounted to 36 per cent. In two of the normal controls whose heat production had been determined, the surface area was actually measured and the errors in Meeh's formula were found to be as follows: E. F. D. B., + 14 per cent., R. H. H., + 7 per cent. In three others, G. L., F. C. G. and L. C. M., the surface area was calculated by the new formula and found to be, respectively, 14.5 per cent., 9.3 per cent. and 13.4 per cent. lower than the results obtained by Meeh's formula. Since in all four cases the new surface area figures are lower than the old results obtained from Meeh's formula, the heat production per square meter of body surface, according to the new formula, would be about 7 to 15 per cent. higher, the average being 39.9. As will be seen in the last two columns of Table 3, the new results are somewhat more uniform than the old results, but are on a higher level, and it is quite possible that it may be necessary to adopt a higher normal average than 34.7. The general principle of Meeh's formula seems to be correct for individuals of average shape, and for this reason it may be used as the standard in large groups of subjects. In the case of very fat individuals, Meeh's formula would give a figure for the calories per square meter which would be much too low. It seems probable that some of the variations from the average normal figure per square meter can be explained by the variable error in the old formula. Future use of the new formula will, it is hoped, clear up this point. The details of the new method will appear in the following paper.

There is but little evidence against Rubner's law that metabolism is proportional to surface area. As we have seen there is a plus error in Meeh's formula for determining surface area. Nevertheless, in a group of normal men of approximately average build between the weights of 45 and 85 kilograms the metabolism is, on the whole, proportional to the surface area as determined by Meeh's formula. When we come to extend Rubner's law to babies and dogs studied in the modern types of apparatus with the modern scrupulous care to exclude the effect of muscular work, we find the figure for the calories per square meter changed, yet not nearly so much changed as the figure for the calories per kilogram of body weight. Murlin and Hoobler[27] have demonstrated that in a group of infants between the ages of 2 and 12 months the metabolism is proportional to weight rather than to surface area, and have pointed out the effect of age, showing that among infants of the same age the metabolism is proportional to the

27. Murlin and Hoobler: The Energy Requirement of Normal and Marasmic Children with Special Reference to the Specific Gravity of the Child's Body, Proc. Soc. Exper. Biol. and Med., 1914, xi, 115.

surface area. Benedict and Talbot[28] believe that the metabolism of infants is not proportional to surface area, but is proportional to protoplasmic mass. Table 7 shows that comparing babies and dogs with adults the method of surface area gives results much closer to the average for men than the method of comparison by weight. It may seem superfluous at this late date to argue at length in support of Rubner's law of surface area, but this law is becoming the center of an active discussion.

The percentage of calories derived from protein in the fasting experiments is a matter of some interest in the discussion of the subject of the toxic destruction of protein. The average figures for the basal experiments on the various subjects are as follows: G. L., 16.5 per cent.; E. F. D. B., 19 per cent.; F. C. G., 18 per cent.; Louis M., 22 per cent.; John L., 15 per cent.; L. C. M., 21.5 per cent. To this list may be added the figures for several normal controls from the work of Benedict and Joslin:[29] F. G. B., 17.6 per cent.; J. R., 15.6 per cent.; J. J. C., 15.7 per cent.; D. B., 21.6 per cent.; H. F. T., 19.9 per cent.; Dr. S., 15.5 per cent.; V. G., 12.7 per cent.; T. M. C., 14.8 per cent. These figures represent largely the effect of the amount of protein in the diet of the preceding day. They are by no means the figures that would be obtained had the subjects been maintained on a protein minimum for a few days before the experiments.

THE EFFECTS OF FOOD

The experiments on the effects of food were intended primarily as controls on the effects of similar meals given to patients with typhoid fever and exophthalmic goiter. While the subject of the specific dynamic action of food is one of great interest and importance it was felt that the chief function of the calorimeter in Bellevue Hospital was the investigation of pathological conditions. Consequently, very simple protein and carbohydrate meals which could be given in typhoid fever were the only ones studied, and the study of the effects of fat was postponed. During the season of 1913 commercial glucose containing dextrose 42.37 per cent., dextrin 44.57 per cent. and water 13.50 per cent. was used. This is one of the cheapest of food-stuffs, is readily soluble in water, is not very sweet and on account of its chemical composition should be rapidly absorbed. It has been found of great service

28. Benedict and Talbot: Studies in Respiratory Exchange of Infants, Am. Jour. Dis. Child., 1914, viii, 1; Gaseous Metabolism of Infants, Carnegie Institution of Washington, 1914, Pub. 201.

29. Benedict and Joslin: A Study of Metabolism in Severe Diabetes, Carnegie Institution of Washington, 1912, Pub. 176, p. 103.

in feeding many of the patients and in some ways is preferable to the less soluble lactose. In the season of 1914 chemically pure dextrose was used in order to compare its effects with that of the mixture. The chief protein meal used in typhoid consisted chiefly of casein in the form of cottage cheese and fat-free milk with the whites of two or three eggs and some egg yolk. It did not make a very palatable mixture, but it was consumed by most of the typhoid patients without much complaint and it certainly did them no harm. While it might have been more satisfactory to give meat, it did not seem justifiable until we had more experience with its effects in fever.

TABLE 7.—COMPARISON OF CALORIES PER KG. AND PER SQUARE METERS OF BODY SURFACE

Investigator	Subject	Calories per Kg.	Calories per Sq. M	Per Cent. Variation from Average for Men: According to Calories per Kg.	According to Calories per Sp.M.
Benedict and collaborators	79 men	1.08	34 7	....	....
Lusk	Dog 1	1.65	31.6	+53	— 9
Lusk	Dog 2	1.75	32.7	+62	— 6
Lusk	Dog 3	1.45	29.8	+35	—14
Lusk and McCrudden	Dwarf, Wt. 21.3 kg.	1.21	32.3	+12	— 7
Howland	Baby 1	2.89	39.5	+168	+14
Howland	Baby 2	3.45	45.7	+220	+31
Murlin and Hoobler	Average 6 infants	2.69	36.3	+150	+ 5
Benedict and Talbot	Average 10 normal in- under 1 month	1.95	25.6	+ 81	—26
	Average 11 normal infants between 1 and 10 months	2.21	35.5	+105	+ 2

Two different methods were used in obtaining a base line to represent the metabolism without food. At first the fasting metabolism was determined in the early morning and the food given while the subject was in the calorimeter. This necessitated a sojourn of three or four hours in the box after the food in addition to the two hours before the food. Even normal individuals become tired after three hours of absolute quiet in a calorimeter and it was evident that patients would be restless in such long experiments. Another disturbing factor was the gradual change in the metabolism with the different hours of the day. The method finally adopted has given great satisfaction. It is the method used so successfully by Lusk[2] on the dog. The basal metabolism is determined in a two- or three-hour experiment and two

days later the food is given before the subject is sealed in the box and the metabolism determined during the same hours studied in the fasting experiment. The basal metabolism in our experience does not change rapidly enough to make this method inaccurate. The high metabolism in the first experiment on E. F. D. B. was due to restlessness, and the low metabolism in the first experiment on F. C. G. was due to profound sleep. Between May 17, 1913, and May 18, 1914, the heat production of E. F. D. B. did not vary 3 per cent. in the three

TABLE 8.—INCREASE IN HEAT PRODUCTION FOLLOWING INGESTION OF DEXTROSE

Subject	Hours After Glucose	Per Cent. Rise	Extra Calories	Extra Calories from Combustion of Carbohydrate	Specific Dynamic Action, Per Cent.
G. L.: 100 glucose............	0-1	20	15.52	.....	..
	1-2	10	8.16	.....	..
	2-3	3	2.26	.....	..
E. F. D. B.: 100 glucose.....	0-1	3	2.63	24.56	11
	1-2	11	8.78	22.88	38
	2-3	9	6.77	20.41	33
	3-4	6	4.28	23.96	18
Total	...	..	22.46	91.81	Av. 25
E. F. D. B.: 200 glucose.....	1-2	13	9.18	41.68	22
	2-3	17	11.73	37.83	31
	3-4	8	5.98	39.22	15
	4-5	7	5.12	40.08	13
Total	...	..	32.01	158.81	Av. 20
L. C. M.: 200 glucose........	1-2	24	15.09	33.37	45
	2-3	16	10.49	41.04	26
	3-4	16	10.25	40.85	25
Total	...	..	35.83	115.26	Av. 31

tests made. In some of the ward patients studied the metabolism has remained constant from day to day and even in typhoid fever has changed in gradual curves. Two hundred grams of dextrose or its equivalent caused an average increase of 12.5 per cent. in the first three to six hours after its ingestion. One hundred grams caused an average increase of 9 per cent. The casein meal with 10.5 gm. N increased the metabolism 12 per cent., the beef with almost 24 gm. nitrogen increased

it 22 per cent.* A more detailed study of the effects of food is given in Tables 8 and 9, which show the effects in the different periods. The percentage increase in metabolism and the extra calories produced are calculated from the nearest basal determination. The extra protein calories produced are calculated from the increase in the urine nitrogen above the average hourly elimination of the nearest basal determination. The extra grams of urinary nitrogen when multiplied by the factor 26.51 give the extra calories from the combustion of protein during that hour. The extra calories produced when divided by this

TABLE 9.—Increase in Heat Production Following Protein Meal

Time After Protein Meal, Hours	Per Cent. Rise in Metabolism	Extra Calories Produced	Extra Protein Calories Metabolized. Extra Urine N × 26.51	Specific Dynamic Action, Per Cent.
E. F. D. B.: 10.5 N				
1½ to 2½	8.0	5.93	8.96	60
2½ to 3½	16.5	12.34	8.27	140
3½ to 4½	12.1	9.08	10.13	90
4½ to 5½	15.5	11.54	1.56	738
5½ to 6½	6.8	5.04	1.56	300
Total	....	43.88	30.48	Av. 144
Louis M.: After 23.93 N				
2 to 3	15.1	9.68	4.80	203
3 to 4	16.2	10.36	4.59	225
4 to 5	28.0	17.94	11.88	151
5 to 6	27.5	17.62	13.04	135
6 to 7	17.6	11.30	16.38	69
7 to 8	25.7	16.45	15.64	106
Total	....	83.35	66.28	Av. 126

figure for the extra protein calories metabolized, give the specific dynamic action in the sense of Rubner (see Note 2, Williams, Riche and Lusk, p. 370), amounting to as much as 144 per cent. and 126 per cent. for the two experiments. The accuracy of this method of calculation may be impaired by the lag in the excretion of nitrogen by

* Since the completion of this paper two more normal men have been given the test meals. Morris S. on Dec. 18, 1914, showed a rise of 6.5 per cent. after a meal containing 9.6 gm. nitrogen. Albert G. on Jan. 6, 1915, showed an increase of 9 per cent. in his metabolism after 115 gm. commercial glucose (100 gm. dry glucose).

the kidneys. In the dextrose experiments the method of calculation is slightly different from the method used by Lusk.[2] The extra calories produced by the combustion of carbohydrate are reckoned as follows: In the nearest basal determination the average figure for the calories per hour is multiplied by the percentage of calories furnished by the combustion of carbohydrate. A similar calculation is made in each hour of the experiment in which dextrose was administered and the extra carbohydrate calories metabolized in each hour determined. This figure divided into the extra calories produced gives the specific dynamic action of 25, 20 and 31 per cent. in the three experiments.

SUMMARY AND CONCLUSIONS

Seven normal men were studied with and without food as controls for the observations on patients in the metabolism ward. Their average basal metabolism (at perfect rest, fourteen to eighteen hours after their last meal) was 34.8 calories per hour per square meter of body surface. The average basal metabolism of 89 normal men studied by Benedict, Emmes, Roth and Smith[10] was 34.7 calories. The average of the 7 men studied in the Sage bed calorimeter in Bellevue and of the 5 men studied in Benedict's bed calorimeter in Boston was 34.2 calories. As a result we have adopted the figure of 34.7 calories per square meter of the body surface as the average heat production of normal men between the ages of 20 and 50 years.

All of the subjects studied in the bed calorimeter were within 11 per cent. of this average. Of the 79 men of normal figure between the ages of 20 and 50 studied by Benedict and collaborators, 86 per cent. were within 10 per cent. of the average and the remainder between 11 and 15 per cent. If, therefore, the heat production of a given subject suffering from some pathological condition is more than 10 per cent. above or below the average it may be regarded as abnormal, but cannot be proved abnormal unless the departure from the average is at least 15 per cent.

Groups of men of weights between 45 and 85 kilograms show a mean heat production within 2 per cent. of the average according to surface area. According to calories per kilogram of body weight the group weighing between 75 and 85 kg. produces 7 per cent. less than the average figure and the group between 45 and 55 kg. produces 9 per cent. more than the average. The conclusion is therefore drawn that among groups of men of varying weights metabolism is proportional to surface area according to Rubner's law and is not proportional to body weight. By using the surface area as a basis one can refer all individuals to a single average normal figure, 34.7. If one uses the body weight as a basis a different normal figure is required for each weight.

The methods of direct and indirect calorimetry in disease agree in two- and three-hour periods; and in health may be found to agree in hourly periods. In the total measurement of 4,577 calories in the experiments reported in this paper the two methods have agreed within 0.17 per cent. In a total of thirty one-hour periods on one normal subject the two methods have agreed within 5 per cent. in twenty-one individual hours and within 10 per cent. in twenty-seven of the periods.

The method of indirect calorimetry using the oxygen consumption as a basis gives the best results in hourly periods. The method of direct calorimetry in short periods is made difficult by uncertainty as to the correct specific heat of the body and also by the fact that the different parts of the body do not always change their temperatures at the same rate. On the average one obtains the best results by considering that the rectal temperature change indicates the mean temperature change of the body, but in typhoid fever the surface thermometers often give a better indication of the mean body change.

The most satisfactory method of determining the effect of food in increasing heat production in normal subjects and patients is to determine the basal metabolism at frequent intervals, and on days shortly after a basal determination administer the food before the subject is sealed in the calorimeter. It has been found that 200 gm. of dextrose or its equivalent in commercial glucose or a casein meal with 10.5 gm. of nitrogen increase the heat production by about 12 per cent. over a period of three to six hours. The basal metabolism of patients with various diseases and the effects of this same food will be discussed in subsequent publications.

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CLINICAL CALORIMETRY

FIFTH PAPER

THE MEASUREMENT OF THE SURFACE AREA OF MAN*

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Recent work on the basal metabolism of infants and adults has revived interest in Rubner's law that heat production in different individuals and species of animals is proportional to the surface area. This law was first definitely formulated by Rubner[1] in 1883, although suggested by Bergman[2] many years before. At the time the experimental work in support of this theory was done no record was kept of body movements and men and animals were allowed to move during the periods of investigation. The average heat production per square meter of body surface was about 1,000 calories per day. In modern work, where the influence of muscular activity is absolutely excluded, the figure is in the neighborhood of 830 calories per square meter per day, as has been shown in Paper 4 of this series. With these new figures it is not unnatural that many investigators have felt that the whole question must be studied anew. Very recently Murlin and Hoobler[3] in New York and Benedict and Talbot[4] in Boston have all concluded that among infants metabolism is more nearly proportional to body weight than to surface area. If this is true for adults, it is a matter of great theoretical and practical importance.

It is obvious that the whole question rests on the accuracy of the determinations of the basal metabolism and of the surface area. The methods of determining the metabolism have been greatly improved, leaving the surface area the doubtful factor. The number of formulas for surface area determination is large, the number of individuals

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* From the Russell Sage Institute of Pathology, in affiliation with the Second Medical Division of Bellevue Hospital.

1. Rubner: Ueber den Einfluss der Körpergrosse auf Stoff- und Kraftwechsel, Ztschr. f. Biol., 1883, xix, 545.
2. Bergman: Wärmeökonomie der Thiere, Göttingen, 1848, p. 9.
3. Murlin and Hoobler: The Energy Metabolism of Normal and Marasmic Children with Special Reference to the Specific Gravity of the Child's Body, Proc. Soc. Exper. Biol. and Med., 1914, xi, 115.
4. Benedict and Talbot: Studies in the Respiratory Exchange of Infants, Am. Jour. Dis. Child., 1914, viii, 1; The Gaseous Metabolism of Infants, Carnegie Institution of Washington, 1914, Pub. 201.

whose area has been measured is small. In 1879 Meeh[5] finished his painstaking and time-consuming work which has remained the standard ever since. He measured six adults and ten children, using a variety of methods. Some parts of the body were marked out in geometrical patterns, which were then traced on transparent paper. The areas of these were then determined by geometry, or, if the pieces of paper were very irregular, by weighing. Some of the cylindrical parts of the body were wound with strips of millimeter paper like a bandage. Funke[6] in one case covered the skin of a cadaver with adhesive material and pasted over this squares of paper. Fubini and Ronchi[7] measured one man by marking out the anatomical regions of the body and determining the areas geometrically. Bouchard[8] used this same method in measuring a number of adults. He speaks of a plan of clothing the body in tights made of some thin, flexible, inelastic sort of paper, the area of which could be determined by weighing. Apparently, he was not able to find the right material. He mentions the fact that M. Bergonie measured surface area by means of plates of lead, and that M. Roussy used a very ingenious cylinder with a revolution counter which he passed over the whole surface of the body. Bouchard also states that D'Arsonval determined the surface area electrically by clothing the man in silk tights and charging him as one would charge a Leyden jar, calculating the surface by applying a metal plate of known area. Lissauer[9] measured twelve dead babies by covering the skin with colored adhesive material and then applying silk paper and measuring the area of the paper geometrically or with a planimeter.

Meeh[5] as a result of his own measurements, based his formula for determining surface area on the fundamental mathematical law that the surfaces of similar solids are proportional to the ⅔ power of their volumes. Using the body weight to represent volume he determined that the constant 12.312 when multiplied by the cube root of the square of the weight in kilograms gave results which came within 7 per cent. of all his measurements of adults and older children. The constant for infants was 11.9 and for various species of animals still different. Miwa and Stöltzner[10] felt the need of introducing linear measurements

5. Meeh: Oberflächenmessungen des menschlichen Körpers, Ztschr. f. Biol., 1879, xv, 425.

6. Funke: Moleschott's Untersuchungen, z. Naturlehre, 1858, iv, 36.

7. Fubini and Ronchi: Ueber die Perspiration der CO_2 beim Menschen Moleschott's Untersuchungen, z. Naturlehre, 1881, xii.

8. Bouchard, Ch.: Traité de Pathologie générale, Paris, 1900, iii[1], 200, 384.

9. Lissauer, W.: Ueber Oberflächenmessungen an Säuglingen und ihre Bedeutung für den Nahrungsbedarf, Jahrb. f. Kinderh., 1902, lviii, 392.

10. Miwa and Stöltzner: Bestimmung der Körperoberfläche des Menschen. Ztschr. f. Biol., 1898, xxxvi, 314.

and chose the height (L) and the circumference of the chest (U) at the level of the nipples in men and just above the breasts in women, retaining the weight (G) as a factor. Using Meeh's measurements they determined by means of the following formula,

$$\text{Surface} = \frac{K\ UGL}{\sqrt[6]{G^4L^4U^2}} \text{ using an average constant (K) of 4.5335.}$$

This formula, which might have been simplified to $\text{Surface} = K\sqrt[3]{U^2GL}$ has never been much used, although its originators have shown that it comes closer to Meeh's cases than Meeh's own formula. Lissauer from the measurement of babies, almost all of whom were atrophic, retained the principles of Meeh's formula, but found that the constant 10.3 gave better results than the constant 11.9. This indicated that Meeh's figure was about 16 per cent. too high. The formula of Miwa and Stöltzner, according to Lissauer, gave no better results than that of Meeh. Howland and Dana,[11] using the measurements of Meeh and Lissauer, have devised a simple formula in which the surface area (y) of the child equals the weight in grams (x) multiplied by a constant 0.483 (m) plus 730 (b). This is expressed in the terms $y = mx + b$.

Bouchard found a consistent plus error in Meeh's formula as given in Table 1. In his own formula, which requires twenty-five pages of tables for its application, he uses the body weight, the height and the diagonal circumference of the abdomen from the hollow of the back to a point somewhere above the umbilicus according to the degree of obesity. Bouchard states that a measuring tape passed around the abdomen and moved back and forth will of itself find the right circumference, which he calls the "tour de taille." Bouchard's formula has been very little used, as it seems to be difficult to understand and apply.

Recently Dreyer, Ray and Walker[12] have made many measurements of birds and small mammals and have found that the surface area, blood volume, cross sections of the aorta and trachea are all nearly proportional to the ⅔ power of the weight. The formula which applies to all these measurements is $S = k\,W^n$, in which S is the surface, blood volume, etc.; k is a constant which varies with the species; W is the weight, and n is approximately 0.70-0.72 instead of 0.666 which would be the ⅔ power. Benedict and Talbot[4] have suggested that the active mass of protoplasmic tissue develops normally on this ratio. They are convinced that metabolism is determined, not by the body

11. Howland and Dana: A Formula for the Determination of the Surface Area of Infants, Am. Jour. Dis. Child., 1913, vi, 33.

12. Dreyer and Ray: Phil. Trans., 1909-10, cci, Series B, p. 133. Dreyer, Ray and Walker: The Size of the Aorta in Warm-Blooded Animals and its Relationship to Body Weight and to Surface Area, Expressed in a Formula, Proc. Roy. Soc., 1912-1913, lxxxvi, Series B, pp. 39 and 56.

surface, but by the active mass of protoplasmic tissue. If both are assumed proportional to the same thing, it will be a difficult matter to prove which is the more important factor.

As shown in Paper 4 of this series, the metabolism of the normal and pathological subjects studied in the Sage respiration calorimeter in Bellevue Hospital has been expressed in terms of calories per square

TABLE 1.—Determination of Error in Meeh's Formula as Applied to Measured Individuals

Subject	Observer	Weight, Kg.	Surface Area as Measured, Sq. Cm.	Constant for Meeh's Formula, Area Divided by Wt.⅔	Error in Meeh's Formula	Age, Yrs.	Height, Cm.	Body Form
Benny L.	D.B. and D.B.	24.2	8,473	10.18	+21	36	110.3	Cretin. Short and fat.
Hagenlocher	Meeh...............	28.30	11,888	12.80	−4	13.1	137.5	Medium strong.
Very thin woman	Bouchard..........	31.8	12,787	12.69	−3	...	....	Very thin.
Korner	Meeh...............	35.38	14,988	13.17	−7	15.7	152	Muscular.
Schneck	Meeh...............	50.00	17,415	12.96	−5	36	158	Very thin.
Adult man	Fobinf and Ronchi	50.00	16,067	11.84	+4	...	....	?
Nagel	Meeh...............	51.75	18,158	12.96	−5	45	160	Somewhat thin.
Fr. Brotbeck ...	Meeh...............	55.75	19,206	13.16	−6	17.7	169	Very strong and muscular.
Naser	Meeh...............	59.50	18,695	12.27	+0	...	170	Somewhat thin, but well proportioned.
Normal man	Bouchard..........	61.6	18,980	12.13	+2	...	....	Normal man.
Fr. Haug	Meeh...............	62.25	19,204	12.01	+2	26.2	162	Strong.
Morris S.	D.B. and D.B.	64.0	16,720	10.45	+17	21	164.3	Short and rather stout.
R. H. H.	D.B. and D.B.	64.08	18,375	11.49	+7	22	178	Tall and thin.
Forstbauer	Meeh...............	65.50	20,172	12.48	−1	66	172	Still very strong.
E. F. D. B.	D.B. and D.B.	74.05	19,000	10.55	+14	32	179.2	Tall, average build.
Normal woman..	Bouchard..........	76.5	19,484	10.81	+14	...	....	Normal woman.
Kehrer	Meeh...............	78.25	22,435	12.26	+0	36	171	Corpulent.
Large man	Bouchard..........	88.6	21,925	11.03	+12	...	....	Large strong man.
Mrs. McK.	D.B. and D.B.	98.0	18,592	9.06	+36	...	149.7	Very short and very fat.
Very fat man...	Bouchard..........	140.0	24,966	9.26	+33	...	....	Very fat man.

meter per hour. The work had progressed but a short distance when it was obvious that no formula based on weight could give the surface area of all the patients with any great degree of accuracy. Among the patients studied were men emaciated from typhoid fever and hyperthyroidism, men of normal shape and men with acromegaluy, hypophysial dystrophy and cretinism. Eventually, it is hoped every conceivable shape will be studied. A formula such as Meeh's is accurate only for objects of different size, *but of similar shape.*

The obvious method for determining surface area is to multiply the length by the average width. An attempt has been made to measure a characteristic length and an average or characteristic circumference of each part of the body and determine the area of the part by multiplying the two and correcting by a constant factor. The sum of the parts will then give the total surface area of the body. When the proper measurements have been selected and the constants for each part determined, it is evident that the method can be applied to individuals of varying shape no matter what disproportion may exist between the different parts of the body.

Fig. 16.—The cretin, Benny L., with mold of his surface area.

INDIVIDUALS MEASURED

The five individuals whose surface area was measured differed from each other in bodily form to a marked degree. All of them had served as the subjects of observations in which the basal metabolism was determined. Benny L. was a cretin 36 years old with the general mental and physical development of a boy of 8. As his photograph (Fig. 16) shows, he was short and stocky, with prominent abdomen, short thick extremities and rather small head. Morris S., 21 years old, was measured three months after he was discharged from the hospital, where he

had been confined three and one-half months with a severe attack of typhoid fever. He had recovered even more than his usual weight in the hospital and during the subsequent stay in the country. At the time he was measured he was of well rounded figure, almost stout. He was short and of small frame, with small hands and feet. R. H. H., a chemist, 22 years old, was tall and thin, with long, slim bones, sinewy muscles and very little subcutaneous fat. E. F. D. B., 32 years old, was tall, but of average build. Mrs. McK. was a very short and very fat woman whose metabolism had been studied in great detail by Dr. David

TABLE 2.—MEASUREMENTS USED IN FORMULA

Index Letter of Part Measured	Benny L.	Morris S.	R. H. H.	E. F. D. B.	Mrs. McK.
A..............	57.5	63.9	65.0	67.0	58.0
B..............	50.2	54.1	56.6	57.8	56.6
F..............	37.2	56.7	65.0	67.3	55.0
G..............	20.2	29.5	27.5	32.5	33.0
H..............	18.7	24.6	26.0	27.5	27.0
I..............	12.8	16.7	16.3	16.2	16.5
J..............	13.6	20.0	21.5	20.2	17.0
K..............	15.2	20.4	20.5	20.5	17.5
L..............	36.6	55.0	55.0	51.5	56.0
M..............	62.0	76.2	72.5	77.0	111.0
N..............	63.5	87.2	85.8	96.0	100.0
O..............	26.4	41.7	47.0	46.3	40.0
P..............	35.5	55.5	54.0	59.0	60.0
Q..............	61.0	96.0	93.2	96.5	117.0
R..............	29.3	41.7	47.0	49.4	36.8
S..............	23.7	35.7	33.8	37.0	41.0
T..............	17.7	24.8	26.2	28.3	21.5
U..............	16.8	22.5	22.2	23.5	19.3
V..............	15.7	21.2	21.2	23.5	22.0

Edsall and Dr. James H. Means in Boston. We are greatly indebted to Dr. Means for taking the measurements of this subject and for taking the mold of the surface and sending it to us to be measured.

MEASUREMENTS OF THE BODY

The individual to be measured was undressed, weighed and placed on a flat table with a vertical foot-board about 30 cm. high. All the measurements were made with the subject flat on his back with his feet against the foot-board. A steel tape was used for all the linear meas-

urements and a cloth tape for the circumferences. The measurements actually used are given in Table 2; those not used are given in Table 3 in case other investigators wish to apply different formulas.

THE MOLD OF THE BODY

The method of determining the surface area finally adopted consisted in making a thin mold of the body, cutting this up in pieces which would lie flat, printing the patterns of these pieces on photographic paper (Fig. 17) and finding the area of the printed patterns by cutting them out and weighing them. The subject was dressed in a tight-fitting suit of thin union underwear, which covered the body, arms and legs. Socks were put on the feet, thin cotton gloves on the hands, while over the head and neck was slipped a section of the leg of a knitted undersuit held in place by means of bandages. On this groundwork strips of paper were pasted until a flexible inelastic mold of the

TABLE 3.—MEASUREMENTS NOT USED IN FORMULA

Index Number of Part Measured	Benny L.	Morris S.	R. H. H.	E. F. D. B.	Mrs. McK.
I............	24.2 kg.	64.0 kg.	64.08	74.49	93.0
II............	110.5 cm.	164.8 cm.	178.0	179.2	149.7
III............	88.8	135.5	148.0	147.2	125.0
IV............	81.1	124.6	136.5	135.5	.....
V............	88.6	124.4	139.0	141.2	125.4
VI............	76.5	115.2	130.0	125.5	107.0
VII............	55.7	83.4	94.0	95.7	76.8
VIII............	46.2	72.3	84.5	85.5	60.2
IX............	65.1	88.5	80.7	84.5	92.0
X............	40.0	60.2	81.5	67.5	55.5
XI............	29.6	43.6	48.0	49.0	40.0
XII............	8.2	11.3	.....	11.7	15.8
XIII............	17.0	24.5	27.0	28.0	21.0
XIV............	21.2	33.1	38.5	38.5	32.0
XV............	18.6	27.5	25.3	30.0	30.5
XVI............	17.8	26.0	25.0	29.0	30.0
XVII............	35.5	50.3	48.0	56.5	56.0
XVIII............	28.2	34.7	32.7	37.5	39.0
XIX............	22.6	31.0	31.5	33.5	30.6
XX............	43.2	52.0	48.0	52.5	35.5
XXI............	28.5	38.0	36.0	37.0	34.2
XXII............	74.5	108.0	99.0	107.0	106.0

body was completed. The material used was strong manila paper, about 1½ inches broad, gummed on one side. It is manufactured in large rolls and is used by stores as a substitute for string in doing up small packages and also by some tailors in making models of their customers. For our purposes it was wound in small rolls and placed in a small brass holder which moistened the gummed side as it was applied to the cloth covering the body. It could be applied so quickly that very little

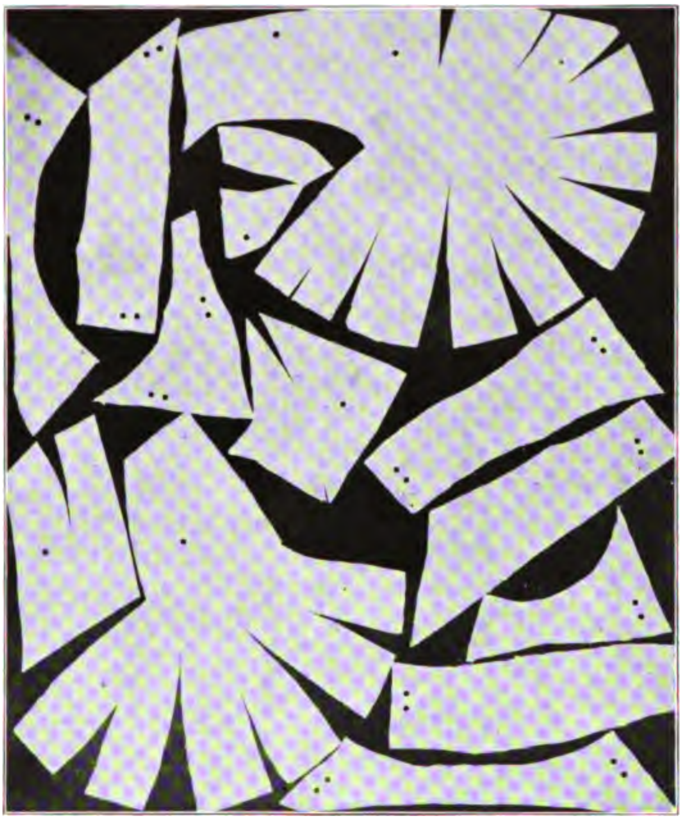

Fig. 17.—Reduced photograph of the patterns printed from the mold of the head and neck of one of the subjects measured. The patterns of the head marked with one punch were cut out and weighed separately from the pieces of the neck marked with two punches. The dark areas were also weighed as control.

time was required to cover the body. The head presented no difficulty until the nose was reached. This region was the last to which the paper was applied and a couple of holes were left for the person to breathe through. The mold of the face was then quickly opened by means of curved bandage scissors. In most cases only one arm and one leg were measured.

TABLE 4.—COMPARISON OF AREAS OF PARTS OF BODY AS ACTUALLY MEASURED AND AS CALCULATED FROM FORMULAS

Part of Body	Benny L			Morris S.			R. H. H.			E. F. D B.			Mrs. McK.		
	Area as Meas-ured, Sq. Cm.	Area as Calcu-lated from Formula, Sq. Cm.	Error in Form-ula, Per Cent.	Area as Meas-ured, Sq. Cm.	Area ac Calcu-lated from Formula, Sq. Cm.	Error in Form-ula, Per Cent.	Area as Meas-ured, Sq. Cm.	Area as Calcu-lated from Formula, Sq. Cm.	Error in Form-ula, Per Cent.	Area as Meas-ured, Sq. Cm.	Area as Calcu-lated from Formula, Sq. Cm.	Error in Form-ula, Per Cent.	Area as Meas-ured, Sq. Cm.	Area as Calcu-lated from Formula, Sq. Cm.	Error in Form-ula, Per Cent.
Head.......	900	888	— 1	1,030	1,064	+3	1,173	1,132	—4	1,154	1,192	+4	1,090	1,010	— 7
Arms.......	1,092	1,074	— 2	2,314	2,236	—3	2,524	2,535	+0	2,776	2,865	+3	2,298	2,351	+ 2
Hands......	596	458	—23*	900	905	+1	968	977	+1	876	918	+5	678	660	— 3
Trunk.....	3,060	3,229	+ 6	6,304	6,318	+0	6,444	6,121	—5	6,572	6,264	—5	7,746	8,303	+ 7
Thighs......	1,284	1,294	+ 1	3,022	3,207	+6	3,712	3,512	—5	3,820	3,655	—4	3,500	3,594	+ 3
Legs........	930	973	+ 5	2,000	2,085	+4	2,396	2,225	—7	2,472	2,560	+4	2,156	2,118	— 2
Feet........	611	596	— 3	1,150	1,123	—3	1,158	1,178	+2	1,330	1,378	+4	1,124	920	—18
Total......	8,473	8,512	+ 0.5	16,720	16,938	+1.3	18,375	17,680	—3.8	19,000	18,832	+0.9	18,592	18,956	+ 2.0

* Benny L. had chronic ulcers on his hands, and the measurement was made with difficulty. The hands of six other individuals were measured and calculated by the formula. The percentage of errors of the calculations in these cases were: —4.0, —1.8, +2.5, —1.8, +2.0 and —2.7.

The hands could not be covered satisfactorily with paper, and hard paraffin was used instead. This was melted and applied to the glove with a brush, soaking well into the meshes of the cotton. The melted paraffin was not too warm for the hands, but was uncomfortable for parts of the body which were not so accustomed to heat. Starch was tried in some instances, but dried too slowly; plaster-of-Paris was too stiff.

Certain portions of the skin were not measured by this mold. The area back of the ears was determined by tracing the back of the ears on a piece of cardboard and correcting by careful measurements. The skin between the toes was measured by tracing. The penis and scrotum were measured and the area determined geometrically. This left unmeasured only very small portions of the face and ears since the mold did not fit closely into the eye-sockets and the concavities of the ear. This error could not have amounted to more than 10 to 20 square centimeters in a total of fifteen thousand.

While the mold was still on the subject the landmarks of the body were located through the paper and the different anatomical regions marked off by drawing the borders on the paper. The mold was then removed with bandage scissors or small probe pointed scissors and the inside of the cloth covered with a thin layer of melted paraffin which, when it hardened, left a material much easier to work with than the cloth and paper alone, since this would not lie flat. Next the mold was cut at the borders of the various regions of the body and each of these regions cut into pieces which would lie flat. These pieces were then marked with a punch for identification and transferred to a large photographic printing frame. After printing in the sun and without developing or fixing, patterns of the pieces of the mold were cut out and weighed to the tenth of a milligram and the blank parts of the sheet weighed as a control. Before this printing each sheet of photographic paper was carefully measured and weighed and the area of each gram of paper determined. By weighing the patterns of each region together it was a simple matter to find the area of that region. A copy of the print made from the mold of the head and neck of one of the subjects is given in Figure 17 showing the method of cutting the paraffined mold so that it would lie flat.

ACCURACY OF METHOD

The accuracy of the procedure was tested in several ways. The bottom of a porcelain evaporating dish was measured twice with a difference of 0.1 per cent. between the two measurements. The surface of the hand of D.D.B. was measured three times, the glove being covered once with starch and on the two other occasions with paraffin.

The square centimeters of surface area as determined on the three occasions were 555.5, 556.0 and 555.5. The right and left sides of the whole body of Benny L. measured separately, agreed within 0.5 per cent.

MEASUREMENTS

The body was divided into the larger regions used by Meeh. An effort was made to select the measurements which represented the length and average breadth of the part. The head region included the ears and the trunk included the neck, the breasts in the female, and the penis and scrotum in the male.

DETERMINATION OF NEW FORMULA

Having measured the surface areas of the different parts of the body and the linear measurements of these parts, the formula to determine the surface area of each part was calculated as follows: the various measurements of length were multiplied by various sums of the measurements representing the width; the resulting figure was divided by the surface area as actually measured. The factors resulting from this calculation in each of the five individuals were compared to determine the percentage variation. That particular combination of length and breadth measurements which showed the smallest variation was chosen and the reciprocal of the average factor for this combination taken as a constant. Fortunately the best results were always obtained by using measurements which were simple. The factors include the multiplication by two necessary to give the area of the right and left arm, hand, etc.

MEASUREMENTS USED IN FORMULA (TABLE 2).

HEAD: AB 0.308.
- A—Around vertex and chin.
- B—Around occiput and forehead, just above eyebrows.

ARMS: F(G + H + I) 0.558.
- F—Outer end of clavicle to lower border of radius.
- G—Circumference at level of upper border of axilla.
- H—Largest circumference of forearm.
- I—Smallest circumference of wrist.

HANDS: JK 2.22.
- J—Lower posterior border of radius to tip of second finger.
- K—Circumference of open hand.

TRUNK: L(M + N) 0.703.
- L—Suprasternal notch to upper border of pubes.
- M—Circumference of abdomen at level of umbilicus.
- N—Circumference of thorax at level of nipples in the male, and just above breasts in the female.

THIGHS: O(P + Q) 0.508.
- O—Superior border of the great trochanter to the lower border of the patella.
- P—Circumference of thigh just below the level of the perineum.
- Q—Circumference of hips and buttocks at level of trochanters.

LEGS: RS 1.40.
R—From sole of foot to lower border of patella.
S—Circumference at level of lower border of patella.

FEET: T(U + V) 1.04.
T—Length of Foot.
U—Circumference of foot at base of little toe.
V—Smallest circumference of ankle.

MEASUREMENTS NOT USED IN FORMULA (TABLE 3)

I—Weight.
II—Height.
III—Sole of foot to suprasternal notch.
IV—Sole of foot to level of nipples.
V—Sole of foot to upper border of axilla.
VI—Sole of foot to tip of ensiform process.
VII—Sole of foot to superior border of great trochanter.
VIII—Sole of foot to perineum.
IX—Circumference of body at level of tip of ensiform.
X—Tip of second finger to upper border of axilla.
XI—Tip of second finger to tip of olecranon process.
XII—Tip of second finger to metacarpo-phalangeal joint.
XIII—Tip of olecranon to lower border of radius.
XIV—Tip of olecranon to outer end of clavicle.
XV—Circumference of arm at the insertion of the deltoid.
XVI—Circumference of arm at belly of biceps.
XVII—Circumference of thigh half way between anterior superior spine of the ilium and the lower border of the patella.
XVIII—Largest circumference of calf.
XIX—Circumference of foot around heel.
XX—From back of neck around superior maxilla just below ears and nose.
XXI—Around neck just below larynx.
XXII—Around shoulders at level of heads of humeri.

BORDERS OF REGIONS OF BODY:
Head: Lower margin of the mandible to its posterior border, thence to tip of the mastoid process and in a straight line to the external occipital protuberance.
Arm: From the acromion process anteriorly and posteriorly to the upper border of the axilla.
Hand: Line at right angles to long axis of forearm drawn at level of tip of ulna.
Thigh: From the perineal point going posteriorly in the natal fold to the upper border of the great trochanter, thence medially in a straight line to the perineal point.
Leg: Line at level of lower border of patella.
Foot: Line at level of tip of lateral malleolus.

DISCUSSION OF RESULTS

Table 1 shows that the constant employed by Meeh has not been confirmed by subsequent observers. It gives results which are too high in every case except one very thin woman. Lissauer found Meeh's figure for infants 16 per cent. too high. Bouchard in four of his five cases found it from 2 to 33 per cent. too high, while in our five cases we have found it from 7 to 36 per cent. too high. The majority of Meeh's

subjects seem to have been thin, and the error of the formula is very great in fat individuals. One can perhaps obtain fairly accurate results in using Meeh's formula if one retains the factor of 12.3 for thin subjects, 11 to 12 for people of average build, 10 to 11 for the moderately stout and 9 to 10 for the very fat. Possibly at some later date a more accurate factor can be determined by the relationship of weight to height, retaining Meeh's fundamental principle of the ⅔ power of the weight.

Miwa and Stöltzner's formula gives results only slightly better than Meeh's. The errors in calculated areas of our five subjects using their formula are as follows: Benny L. + 18 per cent., Morris S. + 17 per cent., R. H. H. + 8 per cent., E. F. D.B. + 18.5 per cent., Mrs. McK. + 26.5 per cent. If the constant of 3.84 were used instead of 4.5335 the results would be much better for this series.

The series of five individuals measured by us is perhaps too small to determine factors which will remain unaltered by subsequent research, but it is doubtful if the changes will be of significance. The range of body shape among our subjects was, however, very great, and the error of the factors comparatively small. The principle of the method has been demonstrated to be sound. Unfortunately, it involves the taking of nineteen measurements, a matter of perhaps fifteen minutes time. Subsequent investigation may reduce the number, but it is difficult to see how one can avoid measuring each part of the body if one wishes to obtain accurate results on people whose shapes do not correspond closely to the average.

In any discussion as to whether metabolism is proportional to body weight or to surface area it is essential to apply a method of measuring the surface which does not depend entirely on weight. The key to the question may perhaps be found in those individuals whose surface area is not proportional to the ⅔ power of their weight, multiplied by a constant determined by measurements of average individuals.

SUMMARY AND CONCLUSIONS

The discussion of the relationship of metabolism to surface area has been based almost entirely on Meeh's formula as determined in 1879. Subsequent observers have found a consistent plus error in this formula amounting to as much as 36 per cent. in the case of very fat individuals.

The surface area of the various parts of the body can be determined as follows: A mold of the surface is made by pasting paper over tight-fitting underwear. The area of the mold is then determined by cutting it in pieces, printing a pattern on photographic paper, cutting out the pieces of the pattern and weighing them.

To determine the area of each part of the body by linear measurements alone a formula has been devised on the principle of length times the average breadth times a constant. The sum of these parts gives the total surface area of the body.

Five individuals of widely varying shapes have been measured and the surface area as calculated from the formulas compared with the surface area as actually measured. In the five cases the average error was 1.7 per cent.

In discussing the question as to whether the basal metabolism is proportional to surface area or to weight it is preferable to determine the surface area by a formula which is not of necessity a function of the weight.

NOTE.—Since this article was submitted for publication the formula has been tested on a tall and exceedingly thin boy, 18 years old. This patient, Gerald S., came to the hospital much emaciated from diabetes and was kept for eleven days practically without food, receiving only whisky. The mold of the body was taken on Dec. 1, 1914, shortly after his fast. At this time he weighed 45.25 kg. His surface area according to Meeh's formula was 1.563 square meters. The mold was kindly measured for us by Miss Margaret Sawyer who obtained the following figures:

	Actual Area as Measured sq. cm.	Area as Calculated from Formula sq. cm.	Error in Formula Per Cent.
Head	950	978	+ 3
Arms	2,052	2,047	— 0
Hands	847	875	— 0
Thighs	3,002	2,677	—11
Trunk	5,003	4,158	—17
Legs	1,876	2,144	+14
Feet	1,042	1,055	+ 1
Totals	14,801	13,934	— 5.8

CLINICAL CALORIMETRY

SIXTH PAPER

NOTES ON THE ABSORPTION OF FAT AND PROTEIN IN TYPHOID FEVER *

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In the course of other work on metabolism in typhoid fever it became advisable to analyze the feces of the patients. While these analyses constitute only a part of the problem in hand, the paucity of studies on the absorption of food in the febrile state appears to warrant publication of the results as a separate communication. For a complete discussion of the absorption of food in typhoid fever the reader is referred to the paper of Du Bois.[1]

Seven cases in all have been studied. The diets administered were modifications of the high calory diet employed in this clinic, that is, the proportions of fat and carbohydrate were varied to satisfy the requirements of the problem under investigation.

METHODS OF CHEMICAL ANALYSIS

Urine and feces were collected in the manner described by Gephart and Du Bois.[2] The analysis consisted in the determination of fat and nitrogen in the feces and total nitrogen in the urine. Nitrogen was determined in all cases by the well known Kjeldahl method, fat in the feces was determined in part by the Kumagawa-Suto method, and later by a saponification procedure described by one of us.[3] Carbohydrate in the feces was not determined (see work of DuBois).

CLINICAL DATA

All of the patients were admitted to Bellevue Hospital during 1913. As is customary on the service, each patient was given an enema every morning. Except when otherwise stated, the patients had from one to two formed or semiformed stools a day.

Emil C., aged 22 years, was admitted August 23, the fifth day of the disease. Widal reaction and blood culture positive. Illness, severe. The original fever lasted twenty-three days. After two days of normal temperature, the patient developed a severe relapse of twenty days' duration.

Thomas B., aged 60 years, admitted October 2, the fifteenth day of the disease. Widal reaction and blood culture positive. Illness, mild. Duration

* From the Russell Sage Institute of Pathology, in Affiliation with the Second Medical Division of Bellevue Hospital.

1. DuBois, E. F.: The Archives Int. Med., 1912, x, 177.

2. Gephart, F. C., and DuBois, E. F.: The Organization of a Small Metabolism Ward, p. 829.

3. Gephart and Csonka: On the Estimation of Fat in Feces, Jour. Biol. Chem., 1914, xix, 521.

TABLE 1.—Daily Averages of Periods

Patient and Weight	No. of Period	Stage of Typhoid Fever	Dates and Days of Disease, Inclusive	Range of Maximum Temp. F.	Food During Period, Averages per Day			Analysis of Feces, Average per Day		Percentage Loss in Feces	
					Carb., Gm.	Fat, Gm.	Nitrogen, Gm.	Fat, Gm.	Nitrogen, Gm.	Fat	Nitrogen
Emil O. ...... 60-62 Kg.	1	Early and late steep curve.	Sept. 11-16 (25-30)	100.6-102.6	162	210	14.9	6.07	1.19	2.9	8.0
	2	Late steep curve..........	Sept. 17-21 (31-35)	99.8-101.0	483	74	15.0	6.30	2.89	8.5	19.3
		Relapse									
	3	Ascend. Temp. and early steep curve.	Sept. 22-Oct. 3 (36-47)	100.0-104.8	331	127	13.6	2.58	1.24	2.0	9.1
	4	Early and late steep curve.	Oct. 4-7 (48-50)	102.0-104.0	174	225	15.0	7.85	2.31	3.5	15.4
Thomas B. .. 74-76 Kg.	1	Contin. Temp.	Oct. 7-10 (20-23)	103.0-104.0	164	211	15.0	9.19	2.09	4.4	13.9
	2	Early steep curve........	Oct. 11-13 (24-26)	102.4-103.0	479	71	14.9	5.80	1.89	8.2	12.6
	3	Late steep curve..........	Oct. 14-16 (27-29)	101.0-103.0	157	204	13.8	5.02	1.28	2.5	9.3
Christian M. 80-82 Kg.	1	Late steep curve..........	Sept. 17-21 (24-28)	100.8-101.8	483	74	15.0	7.04	2.38	9.5	15.9
	2	First week conval.	Sept. 22-25 (29-32)	99.0- 99.6	160	210	15.1	6.85	1.62	3.3	10.7
	3	First week conval.	Sept. 26-28 (33-35)	99.0- 99.4	431	165	16.6	7.60	1.97	4.6	11.9
Ernest H. ... 91-92 Kg.	1	Early steep curve.........	Sept. 20-23 (18-21)	101.2-103.0	160	212	15.4	7.08	1.83	3.3	11.9
	2	Late steep curve..........	Sept. 24-27 (22-25)	100.4-101.6	479	71	15.0	3.75	1.67	5.3	11.1
	3	First week conval.	Sept. 28-Oct. 1 (26-29)	99.8-100.0	226	286	15.3	6.53	1.47	2.3	9.6
Anton K. .... 50-52 Kg.	1	Contin. temp. and early steep curve.	Oct. 7-10 (16-19)	103.8-104.6	47	273	15.0	6.61	1.37	2.4	9.1
	2	Early and late steep curve	Oct. 11-16 (20-25)	99.8-103.8	396	56	12.0	3.93	1.24	7.0	10.3
Richard T. .. 86 Kg.	1	Early steep curve.........	Oct. 17-25 (18-26)	101.0-104.2	285	57	14.3	1.63	0.84	2.9	5.8
Morris S. .... 49.8 Kg.	1	Early steep curve.........	Oct. 30-Nov. 5 (20-26)	102.2-104.0	309	143	15.6	9.74	2.60	6.8	14.8

of original fever, thirty-one days. After fourteen days of normal temperature the patient developed a relapse which lasted twenty days. The relapse was complicated by acute fibrinous pleurisy.

Christian M., aged 31 years, admitted September 8, the fifteenth day of the disease. Widal reaction and blood culture positive. Illness, mild. Duration of fever thirty days.

Ernest H., aged 30 years, admitted September 16, the fourteenth day of the disease. Blood culture and Widal reaction negative, though clinically the disease was undoubtedly typhoid fever. The illness was mild, the fever lasting twenty-four days.

Anton K., aged 18 years, admitted September 30, the ninth day of the disease. Blood culture positive. Illness, severe. Duration of fever twenty-five days. The patient suffered from diarrhea from the eleventh to the sixteenth day, passing three to nine stools a day. The first period of the analyses was not begun until the diarrhea had ceased.

Richard T., aged 14 years, admitted October 6, the seventh day of the disease. Widal and blood culture positive. Illness, severe. Duration of fever twenty-eight days. Mild cholecystitis developed on the twenty-fifth day. After one day of normal temperature a relapse occurred which lasted one week.

Morris S., aged 21 years, admitted October 17, the seventh day of the disease. Blood culture positive. Illness severe. Duration of fever thirty-four days. The patient suffered two relapses, the first severe, beginning on the thirty-sixth day and lasting twenty days; the second mild, beginning on the sixty-eighth day and continuing nine days.

TABLE 2.—DAILY AVERAGES AND PERCENTAGE LOSS

Stage of Disease	No. of Periods	Av. Food Fat Gm.	Average Daily Loss		Percentage Loss	
			Fat, Gm.	Nitrogen, Gm.	Fat	Nitrogen
Cont'd temperature	3	204	6.11	1.20	2.9	10.7
Low fat, steep curve..........	6	67	4.74	1.82	6.9	12.5
High fat, steep curve.......	5	199	7.15	1.84	3.8	11.9
Convalescence	3	220	6.99	1.69	3.4	10.7
Totals	17	...	6.25	1.57	4.3	11.2

DISCUSSION OF RESULTS

In Table 1 the results are expressed in terms of daily averages for the periods, which lasted from three to twelve days. The stage of the disease is designated by a description of the character of the temperature curve rather than by the actual day of the illness. As in previous papers, the stage of ascending temperature corresponds to the "first week," that of continued temperature to the "second week," that of the early steep-curve to the "third week," and that of the late steep-curve to the "fourth week." In the last two columns the losses are expressed in terms of percentage.

A summary of all the periods, in daily averages according to the stage of the disease, is given in Table 2.

ABSORPTION OF FAT

The total fat in the stools varied from 1.63 to 9.74 gm.

The mere statement of the amounts, however, conveys but little information; the stage of the disease and the quantity of fat in the food must be taken into consideration for a complete interpretation of the results. Likewise it should be stated that the expression of the results in percentage values is apt to be misleading unless one bears in mind that even the stools of fasting persons contain fat.

In the ascending and continuous temperature stages when the fat in the food varied from 127 to 273 gm. the total fat lost was from 2.53 to 9.19 gm. The percentage loss varied from 2.0 per cent. to 4.4 per cent.

The average total loss for this stage of the disease was 6.11 gm.; the average percentage loss was 2.9 per cent.

The results in the early and late steep-curve stages fall into two groups, according to the amount of fat which the patient received in his food.

Patients receiving from 56 to 74 gm. lost in the stools from 1.63 to 7.04 gm. of total fat, with an average loss of 4.4 gm. Attention should be directed to the unusually small loss of 1.63 gm. when the patient received 57 gm. The average percentage loss for this group was 6.9 per cent.

With patients receiving from 143 to 225 gm. of fat in the food, the total loss varied from 5.02 to 9.74 gm., with an average loss of 7.15 gm. In this group the relatively large loss of 9.74 gm. when the patient took only 143 gm. in the food should be noted. The average percentage loss for the group was 3.8 per cent.

In convalescence the total fat intake varied from 165 to 286 gm. The fat loss varied from 6.53 to 7.60 gm. The percentage loss was from 2.3 per cent. to 4.6 per cent.

If only those periods be considered in which the fat intake was relatively large, the percentage fat loss in the stools for all stages of the disease was 3.5 per cent. The loss in the febrile stage was 3.3 per cent., in convalescence it was 3.4 per cent. In other words, the patients in this series absorbed fat as well in the febrile stage of the disease as in convalescence.

The average fat loss for all the patients in all stages of the disease amounted to 4.3 per cent. This result is somewhat lower than that obtained by Du Bois, who found the average percentage loss to be 6.02 per cent. When the results are considered as a whole the conclusion appears to be warranted that fat is almost completely absorbed when given in very large quantity.

THE ABSORPTION OF PROTEIN

The quantity of protein in the diet was kept as nearly uniform as circumstances permitted. The lowest daily average intake of nitrogen was 12.0 gm., the highest was 16.6 gm.

The total nitrogen in the stools varied from 0.84 to 2.89 gm. The average total nitrogen for all stages of the disease amounted to 1.57 gm. The highest average loss, according to periods, of 1.84 gm. a day occurred in the steep-curve stage. The smallest average loss of 1.20 gm. occurred in the stage of continued fever. The quantity of fat in the food appeared to be without influence on the nitrogen loss.

The average percentage loss of nitrogen according to periods varied from 10.7 per cent. to 12.2 per cent. The average percentage loss for all stages of the disease was 11.2 per cent. This result is higher than that obtained by Du Bois, which amounted to 7.1 per cent. No explanation of this difference has been found.

SUMMARY

The feces of seven typhoid patients on the high calory diet have been analyzed for fat and protein in seventeen periods of three to twelve days each in length.

The average total fat loss for all the periods was 6.25 gm., corresponding to a percentage loss of 4.3 per cent. No differences were observed in the percentage absorption of fat in the early and later stages of the fever or up to the end of the first week of convalescence, when the intake was relatively large.

The average total nitrogen loss for all the periods amounted to 1.57 gm., corresponding to a percentage loss of 11.2 per cent.

The constant presence of fat and nitrogen in the feces, even in fasting, vitiates to some extent the validity of the results when expressed in percentages.

CLINICAL CALORIMETRY

SEVENTH PAPER

CALORIMETRIC OBSERVATIONS ON THE METABOLISM OF TYPHOID PATIENTS WITH AND WITHOUT FOOD*

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1. Previous investigations.
2. Methods used.
3. Case histories.
4. Experimental data.
5. Discussion of results.
   A. The law of the conservation of energy in fever.
   B. The basal metabolism in typhoid fever.
   C. The specific dynamic action of food in typhoid fever.
   D. The relationship of heat production and heat elimination.
   E. A comparison of caloric intake and caloric output.
   F. Summary and conclusions.

PREVIOUS INVESTIGATIONS

In a previous communication[1] the respiratory metabolism of typhoid patients as determined by means of the small Benedict respiration apparatus was discussed in detail. The literature of the subject was also reviewed, making repetition here unnecessary. Following this earlier work it was possible to continue the study of the typhoid patients by using the respiration calorimeter of the Russell Sage Institute of Pathology in Bellevue Hospital. In the immediately preceding papers of the series[2] the calorimeter and the metabolism ward have been described in detail and data have been given in regard to the normal controls and the absorption of food in typhoid fever. The patients studied were all in the metabolism ward and the calorimeter experiments were conducted in the manner described in the paper on normal controls. In our previous work on the general effect of the high calory diet on respiratory metabolism it was difficult to control the nourishment of the patients so as to determine the basal metabolism and the quantitative effects of different foods. It was, however, pos-

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* From the Russell Sage Institute of Pathology in affiliation with the Second Medical Division of Bellevue Hospital, New York.

1. Coleman and DuBois: The Influence of the High Calory Diet on the Respiratory Exchanges in Typhoid Fever, The Archives Int. Med., 1914, xiv, 168.

2. Clinical Calorimetry, Papers 1 to 6, this number. Brief preliminary reports were published in Jour. Am. Med. Assn., 1914, lxiii, 827, and ibid., 1914, lxiii, 932.

sible to demonstrate that the heat production of typhoid patients on a liberal diet was practically the same as that of fasting patients.

Patients with fever have been studied before in various calorimeters. Isaac Ott[3] of Philadelphia as early as 1892 made observations on a patient with malaria using a rather simple type of calorimeter which required a plus correction of 16 per cent. Likatscheff and Avroroff[4] in 1902 made classical experiments on a similar case. In 1909 Benedict and Carpenter[5] studied a few cases of mercurial poisoning with fever in the Middletown calorimeter. An excellent summary of the literature is given in the Russian publication.[4] It is sufficient to say that the rise and fall of body temperature have been ascribed at various times to every possible combination of increase and decrease in heat production and heat elimination. The Russians used the Paschutin calorimeter in which the patient was kept for twenty-two hours, feeding herself and apparently moving about the chamber during the day whenever she felt inclined to do so. The heat elimination was measured in periods of two hours each and the body temperature was determined every two hours, apparently by means of a mercurial thermometer in the axilla. The CO_2 and water elimination were measured in two-hour periods but the oxygen consumption and consequently the respiratory quotient could only be determined by the change in body weight during twenty-two hours. This method seems to have given satisfactory results, since the quotients correspond to those usually found under similar conditions and calculation of the indirect calorimetry in the three experiments gives results which come within —6 per cent. +6 per cent. and +12 per cent. of the direct calorimetry. The Russians themselves calculated the total heat production by adding the calories stored in or lost from the body as the temperature rose and fell to the calories eliminated by means of radiation, conduction and vaporization. They came to the conclusion that the rise of body temperature was due to an increase in heat production. Benedict and Carpenter studied their fever patients under similar conditions, but determined the oxygen, CO_2 and the heat elimination in periods from two to six hours in length. If one takes the periods when their subjects

3. Ott, Isaac: The Modern Antipyretics, Ed. 2, Easton, Pa., 1892; Fever, Its Thermotaxis and Metabolism, New York, 1914.

4. Likatscheff and Avroroff: Investigations of Gaseous and Heat Exchange in Fevers. Reports of the Imperial Military Academy, St. Petersburg, 1902, v, parts 3 and 4. We are indebted to Dr. F. G. Benedict of the Carnegie Nutrition Laboratory for permission to consult his translation of this important work. Excellent abstracts in English have been published in a paper by A. I. Ringer (Physiology and Pathology of Fever, Am. Jour. Med. Sc., 1911, cxlii, 485) and in the monograph on Fever by Ott.

5. Benedict and Carpenter: Preliminary Observations on Metabolism During Fever, Am. Jour. Physiol., 1909, xxiv, 203.

had a body temperature of 38 C. or over and calculates the indirect calorimetry, using the oxygen and quotients, it is easy to determine the divergence of the direct from the indirect calorimetry. The percentage differences are as follows: +5. +10. —9 +9. +2.

METHODS USED

The present work with the calorimeter was undertaken to extend the previous observations and clear up some doubtful points which could be settled only by a most careful control of the diet and by a comparison of the direct and indirect calorimetry. The fact that it was impossible to bring typhoid patients into nitrogen equilibrium unless the diet greatly exceeded the heat production as calculated from the oxygen consumption, suggested the possibility that the method of calculating the indirect calorimetry might be incorrect. There remained also the old work on fever in which abnormally low respiratory quotients were obtained, leading several investigators to believe that the metabolism in fever was radically different from that in health. Finally, it was hoped that it would be possible to determine whether the rising body temperature was due to an increasing heat production or to a decreasing heat elimination.

The subjects studied were typhoid patients who entered Bellevue Hospital in 1913 and 1914. There was some selection of cases in an effort to obtain men in the early stages of the disease who were intelligent enough to cooperate. Most of the patients were taken to the metabolism ward so early in the disease that it was impossible to predict whether the fever would run a mild or severe course. Several patients were transferred from the First Medical Division through the kindness of Dr. Norrie and Dr. Miller to whom we are much indebted.

All of the patients were put on the high calory diet described in previous publications[6] and trained to take the large amounts of food. The very large amounts formerly given to some patients were not administered and the calories seldom exceeded 3,000 a day. An attempt was made to keep the food nitrogen at 15 grams. The stools exceeded two a day only on the occasions mentioned in the histories, and there was seldom abdominal distention. None of the patients was tubbed, although cold sponges were occasionally given to make the patient

6. Shaffer and Coleman: Protein Metabolism in Typhoid Fever, The Archives Int. Med., 1909, iv, 538-600; Coleman: Diet in Typhoid Fever, Jour. Am. Med. Assn., 1909, liii, 1145; The High Calory Diet in Typhoid Fever — A Study of One Hundred and Eleven Cases, Am. Jour. Med. Sc., 1912, cxliv, 659; DuBois: The Absorption of Food in Typhoid Fever, The Archives Int. Med., 1912, x, 177; Coleman: Weight Curves in Typhoid Fever, Am. Jour. Med. Sc., 1912, cxliv, 659; Diet and Metabolism in Fever, Trans. Fifteenth Internat. Cong. on Hyg. and Demog., 1912.

feel more comfortable when the temperature reached 104. Nervous symptoms were not prominent in any case, although one or two of them were mildly delirious for a few days. Most of the patients were cheerful throughout their illness and read the daily papers. It is estimated that their activity increased their metabolism about 10 per cent. above the basal level, although this figure is necessarily only an approximation.

CASE REPORTS

CASE 1.—Morris S. (severe typhoid) tailor, English Hebrew of Russian extraction, 21 years old, admitted October 17, discharged January 30.

History.—Previous history unimportant; patient is not alcoholic. He landed from England Sept. 28, 1913. October 10 he began to suffer from pain in his abdomen, chest and back. On the thirteenth he had a nose bleed. Since the onset of symptoms he has had no appetite and has been constipated.

Physical Examination.—Patient is a well-nourished young man of small frame and short stature, being 164 cm. tall. There is slight cyanosis of lips and ears, the tongue is heavily coated, tonsils hypertrophied and congested. There is an occasional subcrepitant râle at the apex of the left lung. The spleen is palpable.

Blood taken October 18 gave a negative Widal test but developed a growth of typhoid bacilli. The spleen edge was felt 4 cm. below the costal margin and a few rose spots were present. October 24 the Widal was positive. The next day there were a few sibilant and sonorous sounds over the chest, clearing up by the twenty-seventh. The patient had been on a diet with high carbohydrate and low fat, and on October 23 and 24 had shown abdominal distention with about four liquid stools a day. The distention and diarrhea ceased when the fat was increased and the very large amounts of carbohydrate stopped. For the next month he had only one or two movements a day. October 30 he became a little irrational and his color was grayish, his pulse soft and very dicrotic. November 3 he was irrational in the calorimeter and wrote several notes about the animals which he saw in his hallucinations. The next day he was in much better condition, the pulse was stronger and his physical condition improved steadily.

November 16 the temperature began to rise after it had been practically normal for five days. He felt perfectly well and was bright and cheerful, in spite of a temperature of 104, until the evening of the eighteenth when he had a sharp pain in the right side of the abdomen. This disappeared the next day. This relapse was almost as severe as the original infection, but the patient was not quite so toxic and was never irrational. The temperature remained normal from December 7 to 17. From November 23 to 26 he had frothy stools but these became formed once more when the fat in the diet was increased.

December 17 a second relapse began and lasted until the 27th. During the period of rising temperature he was somewhat apathetic and suffered from headache and was fretful during the two days of high fever. His general condition remained excellent and he never realized that he was having a relapse. Following this, convalescence was rapid, since he had lost practically no weight during his illness. During the next year he reported at the hospital several times, always in excellent condition and five or ten pounds heavier than ever before in his life.

In December, 1914, he returned to the metabolism ward for two days, giving us the opportunity to determine his basal metabolism and the specific dynamic action of the protein meal.

This history is given in detail since Morris S. was placed in the calorimeter twenty-four times. He was an exceptional patient, in that he ate the prescribed diet practically every day and enjoyed the distinction of going in the calorimeter more often than his fellow patients. Nothing made him happier than the extra attention he received on calorimeter days, and as a result he did exactly what he was told to do. We were particularly fortunate in being able to determine the specific dynamic action of protein and the basal metabolism while he was in perfect health, a year after his infection.

Case 2.—Charles F. (severe typhoid), elevator constructor, born in New York, 24 years old, admitted November 4, discharged January 12.

History.—Lives in same house as his nephew Howard F., who has similar symptoms. On October 28 he began to suffer from anorexia, malaise and headache. On November 3 he had a nose bleed. He did not take to bed until admitted to the hospital.

Physical Examination.—Fairly well-nourished young man of medium frame, 166 cm. tall. He is moderately prostrated; there are several rose spots and the spleen edge is palpable 4 cm. below the costal margin.

Blood taken the day after admission gave a positive Widal test and showed a growth of typhoid bacilli. November 7 and again on the eighth he had a small intestinal hemorrhage of about 200 c.c. His general condition remained fair; he was rational and the toxemia not marked. He was given a daily sponge for his high temperature. At this time he took his food very badly and after the hemorrhages ceased it was impossible to give even 2,000 calories. November 14 to 17 he had a severe follicular tonsillitis and his toxemia was marked. Rose spots appeared in crops. On the nineteenth he had a hemorrhage of about 250 c.c. and was very toxic and apathetic for the next week. His pulse was very soft, systolic blood pressure being 95 mm. mercury. By December 3 the temperature was normal, he was much improved and was reading the paper every day. Convalescence was rapid. Throughout the disease he had one formed stool each day.

This patient was very intelligent and was anxious to help us in every way possible but his digestion made it difficult for him to take the food. He was very quiet while in the calorimeter.

Case 3.—Howard F. (typhoid fever of moderate severity), schoolboy, born in New York, 12 years old, admitted November 4; discharged January 22.

History.—Lives in the same house as his uncle, Charles F. He was perfectly well until October 26 when he had a severe headache. On the twenty-eighth he felt so sick that he took to bed. The next day he had a chill; vomited. He had nose bleed on the thirty-first and on the day of admission.

Physical Examination.—Patient is a tall, slender boy who has not yet reached the age of puberty; height 160 cm.; the cheeks are flushed and he looks acutely ill. Heart apex in the fourth space 8.5 cm. to the left of the midline. There are several rose spots on the abdomen; the spleen is not palpable.

On November 14 the blood culture showed typhoid bacilli. November 12 showers of subcrepitant râles appeared at the left base and the next day sibilant and sonorous sounds were heard all over the chest. His general condition was good, and although he was very apathetic, he was perfectly rational. He took his food very poorly, vomiting often. By the seventeenth he was very thin, quite toxic, very drowsy but rational. The pulse was soft but of fair quality.

The sibilant and sonorous sounds persisted until the twenty-fourth, by which time the temperature was falling, the appetite much better and the patient able to read the paper. Convalescence progressed rather slowly. On December 10 he passed two ascarides. The heart action was rapid on exertion and on the eighteenth the apex was in the fourth space 9.5 cm. from the midline. He left the hospital in good condition. Throughout his illness he had one stool a day.

The boy was very intelligent and made a good subject for the calorimeter.

Case 4.—Karl S. (typhoid fever of moderate severity), stoker on steamer to South America, German, 24 years old, admitted December 29; discharged Feb. 18.

History.—Returning on a voyage from Brazil he landed at San Domingo for a few days, reaching New York December 20. Two days later he began to suffer from headache, weakness, lassitude, anorexia and nausea. On the twenty-fourth he began to have daily chills.

Physical Examination.—One hundred and sixty-eight cm. tall, muscular and well nourished. His face is flushed and he looks stuporous. No spots, spleen not palpable. Blood taken the day after admission gave a negative Widal but positive growth of typhoid bacilli. January 1 rose spots appeared and the spleen became palpable. On the third he was prostrated, apathetic and showed slight subsultus tendinum. The pulse was soft and dicrotic and the abdomen distended. When carbohydrates were pushed too high he became distended, but this trouble disappeared when the amounts were decreased. By January 7 he was anxious about his condition and easily frightened. On the tenth his condition was satisfactory and by the twenty-sixth he was afebrile and was reading and studying every day. He was very hungry during his rapid convalescence. February 14 he developed tonsillitis. The temperature rose to 101 and the pulse became rapid. He did not feel sick and resented being confined to bed. On the seventeenth he became insubordinate and was discharged from the hospital. Two weeks later he returned on a visit in good condition.

This patient was a rough sailor of sullen disposition and made a rather restless subject for the calorimeter. During most of the observations on this man one of the water thermometers was being repaired and the method of direct calorimetry could not be used.

Case 5.—Thomas B. (typhoid fever, mild; followed by acute fibrinous pleurisy). Laborer, Irish, 60 years old, admitted October 2, discharged December 8.

History.—Moderately alcoholic. About September 18 began to suffer from malaise, anorexia and fever.

Physical Examination.—Large well-nourished man, who looks acutely ill. He is apathetic and slightly cyanotic.

Blood taken the day of admission gave a positive Widal and showed a growth of typhoid bacilli. Many rose spots appeared but the spleen was never palpable. He took his food well and was never very ill. From October 22 to November 6 the temperature was normal. Then it rose gradually to 104 and fell slowly reaching normal on the twenty-sixth. During this time he developed dulness, bronchial voice and breathing at the left base, the signs being attributed to a pleurisy rather than pneumonia. He made a rapid convalescence.

Case 6.—Richard T. (mild typhoid). Mulatto boy, born in New York, 14 years old, admitted October 6, discharged November 24.

History.—About September 30 began to suffer from headache, weakness, constipation and occasional abdominal pains.

Physical Examination.—Well nourished active boy who has not yet reached puberty. There are a few rose spots and the spleen is palpable.

The day after admission the blood culture gave a positive Widal and showed a growth of typhoid bacilli. The disease ran a mild and uneventful course, in spite of high evening temperatures, until October 25, when he developed slight pain and tenderness over the gall bladder, lasting two days. The temperature reached normal October 29, but rose again in a mild relapse lasting till November 6. Convalescence was rapid.

The boy was somewhat mischievous and was very active throughout his stay in the hospital. While in the calorimeter he spent most of his time looking out of the window and was not as quiet as most of the patients.

CASE 7.—Anton K. (mild typhoid), factory worker, Austrian, 18 years old, admitted September 30, discharged November 18.

History.—September 22 he began to have daily chills and fever, lost his appetite. felt exhausted and had severe pains in the epigastrium.

Physical Examination.—This showed a well-nourished man, apathetic and acutely ill. Typhoid bacilli were found in the blood. At the height of his fever he was prostrated and developed slight subsultus tendinum. He took his food well and was in good condition on October 16, the first day of normal temperature.

CASE 8.—Rose G. (severe typhoid), born in New York, 12 years old; admitted September 19, discharged November 26.

History.—Menstruation has not yet begun. The girl is tall and very thin and is somewhat deficient mentally. She went through a severe course of typhoid, with marked emaciation. Blood culture showed typhoid bacilli. During the disease she had râles at both bases and developed bed sores because she had all her life been incontinent of urine. Temperature reached normal October 29, and she was up and about on November 17. During convalescence she ate enormous amounts of food, with very slight gain in weight. She was not in the metabolism ward and exact figures for the food were not obtainable, but it seemed as if the discrepancy between food and gain in weight could be accounted for only by a greatly increased metabolism. The first hour she was in the calorimeter she was quiet, but during the second hour she voided in bed and began to cry, making it necessary to end the observation.

CASE 9.—Edward B. (severe typhoid), longshoreman, born in Ireland, 36 years old; admitted October 3, 1914, discharged February, 1915.

History.—He remembers no previous illnesses. October 1 he began to suffer from headache, pains all over the body and abdominal cramps, with diarrhea and three to four stools a day. He had no nausea and the appetite was good.

Physical Examination.—Well-nourished man of medium frame, fairly muscular. He is dull and apathetic and moderately prostrated. The heart is rapid, not enlarged, the lungs are clear, abdomen soft, spleen palpable. There are a few rose spots.

The blood on October 4 was sterile, but gave a positive Widal test. On the sixth he was very drowsy; by the tenth he was comfortable and eating well. October 13 the temperature had again risen, the pulse rate had jumped to 120 and the quality of the pulse was poor. On the twentieth he was much better and was taking his food well, but the abdomen was slightly distended. By November 1 the temperature was almost normal and the general condition excellent in spite of a small rapid weak pulse. By November 7 the temperature was up again, and he was beginning to feel indisposed. The appetite was poor and the pulse rate between 138 and 148. During the next few days the pulse was very rapid, slightly irregular, and very weak. He was very toxic but was rational except for short periods when the mind was a little hazy. November 16 he had a small hemorrhage with a short period of collapse, but recovered quickly. His condition improved steadily until December 3 when the temper-

ature rose once more and he suffered from a moderately severe relapse, lasting until December 21. Following this was a period of three days of normal temperature and then a fourth relapse, very mild in character lasting only three days. During the whole period of his illness his nutrition remained good; he was always cheerful and read the newspaper almost every day.

CASE 10.—John K. (typhoid fever, mild), deck hand, Polish, aged 35; admitted Dec. 12, 1914, discharged Jan. 27, 1915.

History.—December 2, began to suffer from malaise. December 5 had a severe chill and took to bed; since then has had chills almost every day. Has had continuous headache, has vomited frequently and has been constipated.

Physical Examination.—Tall and thin, fairly muscular. Tongue dry, coated, fissured. Heart and lungs clear, spleen palpable, many rose spots.

December 12, the blood culture was sterile but the Widal positive. On the thirteenth he had his last chill, on the sixteenth he was apathetic and prostrated, pulse was slow and dicrotic, there was a patch of herpes on the upper lip. As the temperature fell during the next few days his condition improved rapidly, but the apathy remained until the temperature was normal, and he was unusually quiet, remaining almost motionless all day long. Convalescence was rapid.

DISCUSSION OF RESULTS

Law of Conservation of Energy in Fever.—The law of conservation of energy has been shown to apply to the lower animals, to normal men and to babies, and has been discussed in the previous paper (Paper 6) on normal controls, in which it was demonstrated that with normal men a satisfactory agreement between the direct and indirect calorimetry could be obtained in periods as short as one hour. While there are few who doubt that the law applies to men with fever, it may not be superfluous to bring forward proof.

An agreement of the direct and indirect calorimetry within the limits of experimental error indicates that protein, fat and carbohydrate are oxidized to the same or approximately the same end products as in health and that in the oxidation they give off the standard amounts of heat. The method of calculating the indirect calorimetry depends on the assumption that the calories furnished by each gram of protein, fat and carbohydrate correspond to the standard figures of Loewy,[7] protein 4.32, fat 9.46, starch 4.18. The results obtained by the method of direct calorimetry, which is dependent only on fundamental laws of physics, must remain the standard method of comparison when considering large groups of experiments. Once the agreement has been proved for the group, the method of indirect calorimetry is preferable for individual experiments as has been shown in previous papers on account of the technical difficulty of the method of direct calorimetry in short periods.

Table 1 gives a summary of the percentage divergence of the direct and indirect calorimetry in all the experiments on the typhoid patients,

7. Loewy: Der respiratorische und der Gesamtumsatz, Oppenheimer's Handb. der Biochem, 1911, iv, 280.

the great majority of them being three hours long. In all cases the indirect method was used as a standard. If we consider the total measurement of 12,822 calories, we find the direct method, as calculated from the rectal temperature, gives results only 2.2 per cent. lower than the indirect. In almost half of the experiments the body temperature was measured by a thermometer of two units strapped on the thorax in the region of the apex of the heart and just below the right nipple, each unit being covered by a pad of cotton about 15 cm. square and 4 cm. thick. The rectal thermometer was inserted about 12 cm. beyond the sphincter. In a previous paper attention has been called to the fact that in these typhoid cases in which both methods were tried

TABLE 1.—PERCENTAGE DIVERGENCE OF DIRECT FROM INDIRECT CALORIMETRY IN THE INDIVIDUAL EXPERIMENTS

Percentage Divergence	Number of Experiments Falling in Each Group					
	According to Rectal Temperature			According to Surface Temperature		
	+ Divergence	— Divergence	Total	+	—	Total
0- 5............	17	22	39	11	7	18
6-10............	3	15	18	2	7	9
11-17............	1	3	4	0	1	1
Total.......	..	..	61	..	..	28
Average Error..	..	..	±4.9%	..	..	±4.0%

	Indirect	Direct*	Divergence
			%
Total calories measured in all experiments...........	12,822.08	12,539.67	—2.2
Excluding first periods...............................	8,470.98	8,488.97	+0.2
Calories measured in febrile experiments excluding all first periods	5,720.21	5,583.55	—2.4

* According to rectal temperature.

slightly better results were obtained by using the surface thermometers to give the temperature changes of the body than by using the rectal. In the long run the rectal thermometer is the more reliable, since it is not so easily displaced by bodily movement, but enough evidence has been accumulated to show that the rectal temperature does not always change in the same degree and not always in the same direction as the average body change. As the body cools off there may be a relative increase in the heat near the surface of the body, since this is the place that most of the heat is dissipated. The opposite takes place when the temperature is rising. On account of the rapid circulation of blood

there is, of course, a tendency for the temperature curves of the different parts of the body to follow the deep temperature as measured in the rectum.

In the sixty-one experiments in which the rectal temperature was measured the average divergence of the indirect calorimetry from the direct calorimetry (as based on the rectal temperature) is only ±4.9 per cent. In twenty-eight of these experiments it was possible to base the calculations on the changes in the surface temperature, with an average divergence of 4.0 per cent. using this latter method. This divergence of 4 or 5 per cent. is not more than one often finds among normal controls, since the technic is difficult even with trained subjects. The reason for the total minus error of 2.2 per cent. is not clear. The largest part of this error frequently falls in the first hour, especially in patients with fever, and we have been led to suspect that the subject continues to give out heat to the wooden bed frame and to the bedding even after he has been on the bed for an hour. If we excluded from our calculations the first periods, while the calorimeter is still coming into thermal equilibrium, we find that the direct and indirect methods agree within 0.2 per cent. If we consider only those experiments made during the febrile period, we find a larger proportion show a minus error in the direct calorimetry than when we take all the experiments put together. Excluding the first hours of each experiment, however, the direct calorimetry gives a total only 2.4 per cent. lower than the indirect. The difference is so small that it might be found in a group of normal controls. It may be entirely accounted for by the difficulty in measuring the average body temperature during fever.

Basal Metabolism in Typhoid Fever.—In Paper 4 of this series the reasons have been given for the selection of the standard of the average normal basal metabolism. The figure of 34.7 calories per square meter per hour as based on Meeh's formula has been used in all the calculations. It was impossible to use the new surface formula as a standard since this was not devised until most of the typhoid work had been completed.

The relationship of the basal metabolism of the typhoid patients in the various stages of the disease to the normal is shown in Table 2. This corresponds in a striking manner with the averages of the fasting typhoid patients investigated by Kraus, Svenson, Grafe and Rolly and collected by us in a previous publication.[1] It is evident from the general trend of the results that the total metabolism increases and falls in a curve roughly parallel with the body temperature, and that the period when it drops below normal in many patients corresponds with the period of subnormal temperature which occurs so often in the first week of convalescence. From a study of the results obtained by the

calorimeter and by various smaller types of respiration apparatus, it is apparent that there is considerable variation in the heat production of different patients and the same patient at different stages of the fever. While we can state that the average increase in typhoid fever is approximately 40 per cent., we must remember that figures over 50 per cent. are frequently encountered. This should make us cautious in drawing too many deductions from feeding experiments unaccompanied by determinations of the respiratory metabolism. It should also be remembered that typhoid fever is the only fever which has been thoroughly investigated and that if variations occur in this one disease the variations may be quite different in other febrile diseases such as erysipelas, pneumonia, puerperal fever, etc.

TABLE 2.—Basal Metabolism, According to Periods of Typhoid Fever

Periods	Number of Patients	Number of Observations	Average Per Cent. Rise Above Average Normal 34.7 Cal. per Sq. M.	Average Respiratory Quotient
Ascending temperature	2	2	+37	0.79
Continued temperature	5	7	+42	0.77
Early steep curve	3	4	+26	0.82
Late steep curve	3	3	+16	0.82
Relapse—				
Ascending temperature	2	3	+25	0.82
Continued temperature	2	2	+51	0.76
Early steep curve	2	4	+36	0.78
Late steep curve	1	1	+16	0.79
Convalescence—				
First week	3	4	— 2	0.91
Second week	3	5	+ 6	0.88
Third week	1	1	+17	0.81
Fourth week	2	2	+15	0.86
Fifth week	2	2	+ 4	0.81

Benedict and his co-workers in all their recent publications have drawn attention to the fact that pulse rate and total metabolism show curves which are roughly parallel. As might be expected this parallelism is not as apparent in typhoid fever as in the conditions they have studied. Typhoid is characterized by a slow pulse in the first two weeks when the metabolism is high. The experiments here reported do not show any striking agreement in the rise and fall of the two curves.

The Specific Dynamic Action of Food.—When studying the effects of the high calory diet in typhoid fever with the small Benedict respira-

tion apparatus, the writers noted the fact that the metabolism of liberally fed typhoid patients was scarcely raised above the metabolism of fasting typhoid patients. The conclusion was drawn that food exhibits little or no specific dynamic action in typhoid fever. One of the chief objects of the present research was to study this striking phenomenon more closely, inasmuch as some observers, among them Von Noorden,[8] have stated that the specific dynamic action of food was increased in fever, exophthalmic goiter and several other conditions.

We have seldom kept typhoid patients in the calorimeter for periods exceeding three or four hours. After this length of time the patients often become restless and bored, making the results unreliable. This

TABLE 3.—Specific Dynamic Action of Protein and Carbohydrate in Health, Fever and Convalescence

Subjects	Number of Experiments	Average Gm. of Nitrogen or Glucose in Food	Average Gm. Food per Kg. Body Weight Nitrogen or Glucose	Average Per Cent. Rise in Metabolism
Protein meal				
Two normal men*	2	10.1	0.147	9.3
Four febrile patients	6	8.6	0.174	4.5
Four convalescents	5	10.2	0.217	16.6
Commercial glucose				
Three normal men*	3	115.0	1.6	9.1
Two febrile patients	4	115.0	2.2	1.0
Three convalescents	3	115.0	2.7	9.8

* Since the completion of Paper 4 two more normal controls have been given the test meals. Morris S. on Dec. 18, 1914, showed a rise of 6.5 per cent. after a meal containing 9.6 gm. N.; Albert G. on Jan. 6, 1915, showed an increase of 9.0 per cent. in his metabolism after 115 gm. commercial glucose.

has made it impossible to determine the basal metabolism in a two hour experiment and follow it immediately by a three or four hour experiment to find out the effect of food. Moreover, in such a long period the temperature might change several degrees, making the results difficult of interpretation. In the case of normal controls, the basal metabolism is so uniform from day to day that very accurate results can be obtained by determining the basal metabolism and the metabolism after food on different days. In fever the change in the level of metabolism from day to day makes the results less accurate but the error will be small if certain precautions are taken. The level of basal heat production changes in a fairly gradual and uniform curve and

8. Von Noorden: New Aspects of Diabetes, New York, E. B. Treat & Co., 1912, p. 20.

there is but a small change in twenty-four hours unless the temperature or the general condition of the patient changes markedly. For this reason the effect of a given meal has been determined sometimes the day before, sometimes the day after and sometimes the day between basal experiments. The protein meal was given six times in the febrile period and the glucose meal four times. It is against the laws of probability that the basal metabolism should take a sudden change in the same direction on all these days.

The fact that the average amount of protein given in the febrile period was less than that given in health was due to the poor appetite of the patients at the height of the disease. Even in health and in

TABLE 4.—CHART SHOWING NEGATIVE NITROGEN BALANCES IN TYPHOID PATIENTS WHO RECEIVE FOOD CALORIES IN EXCESS OF CALCULATED HEAT PRODUCTION

Patient	Dates or Days of Disease Inclusive	Days in Period	Range of Maximum Temperature, Degrees F.	Calculated Heat Production, Cal.*	Food Calories*	Food N, Gm.*	Nitrogen Balance Gm.*
Morris S.	Oct. 23-Nov. 3	12	102.8-104.6	2,266	2,863	16.4	—4.4
	Dec. 19-24	6	101.9-105.1	2,085	2,989	18.2	—2.4
Charles F.	Nov. 28-30	3	101.2-103.4	1,752	2,458	12.0	—4.6
Karl S. ...	Jan. 12-18	7	101.0-105.0	2,197	2,985	16.1	—3.2
	Jan. 19-22	4	98.8- 99.0	1,678	2,819	14.6	—1.9
John K....	Jan. 15-20	6	103.2-104.0	2,568			
Frank W.†	Days of Disease 11-14	4	104.0-105.4	2,200	2,250	11.3	—5.0
	15-19	5	103.0-104.0	2,238	3,320	15.3	—3.3
	20-23	4	101.0-103.6	2,054	2,362	15.9	—1.5

* Figures given are averages for twenty-four hours.
† Taken from Coleman and Du Bois.[1]

convalescence the meal is a large one, containing almost as much protein as most people consume in a day. We must remember also that the normal controls weighed 75 and 63 kg. when they took this meal and that the typhoid patients weighed 51, 58, 35, and 54 kg., respectively. As is shown in Table 3 the controls received less nitrogen per unit of body weight than the fever patients. We can therefore state that protein and glucose exhibit a much smaller specific dynamic action in typhoid fever than in health, while in convalescence from the disease the specific dynamic action seems to be greater than normal. In the case of glucose there was practically no specific dynamic action in fever, and in the case of Morris S. the specific dynamic action of the protein was very slight.

The cause for this phenomenon has not yet been definitely ascertained but the most plausible theory was stated by Dr. Graham Lusk[9] in the discussion on the symposium on nutrition at Atlantic City in 1914. He called attention to the well known fact that if the metabolism be increased by lowering the environmental temperature there may be

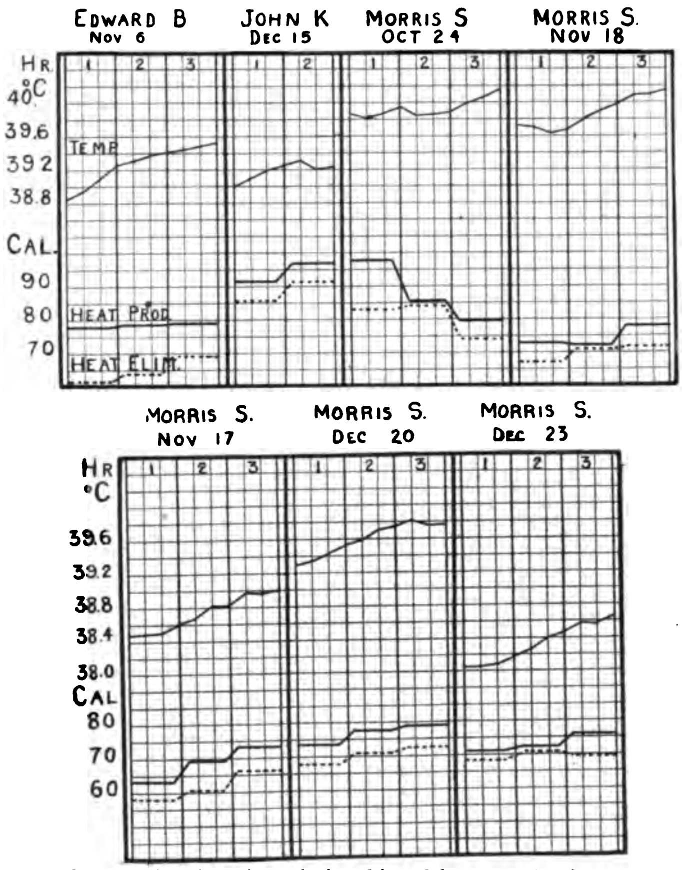

Chart 1.—Curves showing the relationship of heat production and heat elimination in fever. Rising temperature. The uppermost line shows the rectal temperature as measured every twenty minutes. The heavy continued line represents the heat production in hourly periods as determined by the method of indirect calorimetry. The dotted line gives the heat elimination as determined by the measurement of the calories of radiation, conduction and vaporization. The difference between the levels of these two lines represents the heat stored in the body as the temperature rises. Note the fact that in every case except one the heat elimination increases with a rising temperature.

no specific dynamic action as usually induced by ingested food. In like manner if the metabolism be raised in fever, food ingestion may cause no increase. He also stated that since protein metabolism in fever

9. Lusk: Jour. Am. Med. Assn., 1914, lxiii. 831, foot of page.

can never be reduced to as low a level as is present in the normal organism, therefore protein ingestion in fever often merely serves to replace the protein already breaking up in increased quantity, and such protein ingestion would not then serve to increase the heat production.

The Regulation of Body Temperature.—The study of the regulation of body temperature is one that demands the utmost accuracy of technic. The question at issue is whether a rise in temperature is due to an increase in heat production or a decrease in heat elimination. Previous investigators have tried to solve this problem on data obtained from the direct calorimetry alone, or from the indirect calorimetry accompanied by measurements of body temperature. In either of these two methods the whole calculation would depend on the exact

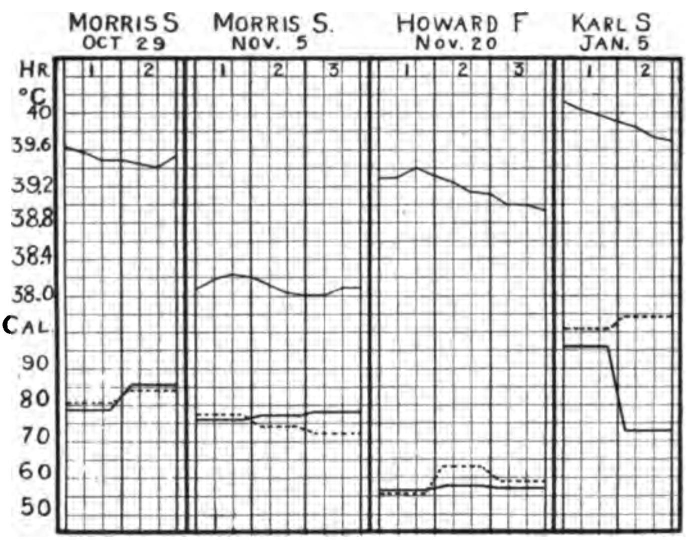

Chart 2.—Curves showing the relationship of heat production and heat elimination in fever. (See legend Chart 1.) Temperature level or falling. In the last two experiments it will be noted that the heat elimination rises above the production.

measurement of the average change in body temperature, the exact calculation of specific heat of the body and the amount of heat stored in or lost from the body. It has been shown in this and preceding papers that these measurements and calculations are the weakest points in the science of calorimetry and it is only very recently that the technic has been so developed that investigators have attempted a comparison of the methods of direct and indirect calorimetry in periods shorter than six to twelve hours, periods obviously too long for the study of the problem in question. If, in a period of experimentation, the results obtained by the method of indirect calorimetry and by the method of

direct calorimetry, using either the rectal or the surface temperature, do not agree within 5 per cent., we must suspect some error, probably in the measurement of the average body temperature change. For this reason we have eliminated from the discussion all experiments in which the two methods do not agree within 5 per cent. It is also preferable to eliminate all experiments after the taking of food and all experiments in which the subject was not quiet. This gives us eleven experiments during the febrile period in which the technic left nothing to be desired.

In Chart 1 are grouped those experiments in which there was a rising body temperature. The dotted line shows the total heat eliminated from the body by means of radiation, conduction and vaporization. The continued line shows the heat production as determined by the method of indirect calorimetry, which does not use a single factor that affects the dotted line. With a rising body temperature the heat production within the body must be greater than the elimination to provide for the storage of heat in the tissues. Many are of the opinion that the rise in temperature is chiefly due to a decrease in the heat elimination. This we find to be the case only in the last hour of one of the seven observations, there being a sharp drop in both heat production and elimination towards the end of the experiment on Morris S. on October 24. In all the other periods the rising temperature was accompanied by an increasing heat production which outweighed the increasing heat elimination.

In Chart 2 which shows periods in which the body temperatures were fairly level the production and elimination were about equal and constant. In the two observations with falling temperature the heat production remained fairly level while the elimination was increased.

Heat Production, Weight and Nitrogen Equilibrium.—In the cases here studied it is possible to make a comparison of the caloric intake and the caloric output. The intake consists of the calories of the food. The output is made up of many factors, but principally of calories lost by radiation, conduction and the evaporation of water. The first and most important consideration is the determination of the basal heat production as measured by the methods of direct and indirect calorimetry. As has been shown above, the two methods agree within 2 per cent. The actual heat production during the different hours of the day can depart from the basal as a result of various factors. We have shown above that the ingestion of large amounts of food causes but a slight increase in metabolism, averaging less than 5 per cent. in the case of protein and only 1 per cent. in the case of carbohydrate. These increases may be considered the maxima since the amounts of foods given were the largest the patient could take and the hours of the

observation were the hours of the greatest specific dynamic action. The exact percentage rise caused by the stimulation of the food taken during the whole day is problematical but may be estimated as about 3 per cent. The percentage of calories lost in the feces has been studied in two previous papers and has been found to be practically normal. The calories lost as urea and in the feces are taken into consideration in the calculation of the fuel values of the food. In the one case in which there was alimentary glycosuria (Frank W.),[1] the calories lost as dextrose have been subtracted from the intake. In a previous paper the writers have discussed the evidence against an abnormal loss of partially oxidized carbon compounds in the urine and have come to the conclusion that this factor is negligible. The entire absence of abnormal respiratory quotients supports this view. The lowest quotient found was 0.72, the highest 1.04, obtained respectively during fasting and high carbohydrate ingestion, and thus exhibiting entirely normal relations.

The most uncertain factor is the variation in heat production caused by changes in the muscular activity. It is quite possible that a patient who is very delirious and very restless might produce twice as many calories as when quiet. The total heat production of such patients could be determined only by the Middletown type of experiment in which the subject was kept in a respiration calorimeter for days at a time. Such experiments are obviously impossible in typhoid fever. The question remains as to whether we obtain a fair sample of the day's metabolism by making two or three observations a week between the hours of 11 in the morning and 2 or 3 o'clock in the afternoon. This period includes some of the morning hours when the metabolism is said to be low and some of the afternoon hours when it is said to be high. During the experiment the activity of the patient has been almost the same as the activity observed in the ward during the greater part of the day between the hours of 5 in the morning and 8 in the evening. In the calorimeter the subjects are allowed to turn from side to side several times during the hour and they shift their position often enough to make themselves comfortable, which is exactly what they do in their beds in the ward. Part of the time they doze and part of the time they are awake and are looking out of the calorimeter window. In the ward they are kept flat in bed and are never allowed to sit up until the temperature has been normal for several days. They are never given cold tubs and hardly ever given cold sponges. Their food is served on trays and they help themselves with a minimum of exertion. In the morning the nurse gives each patient an enema, sponges

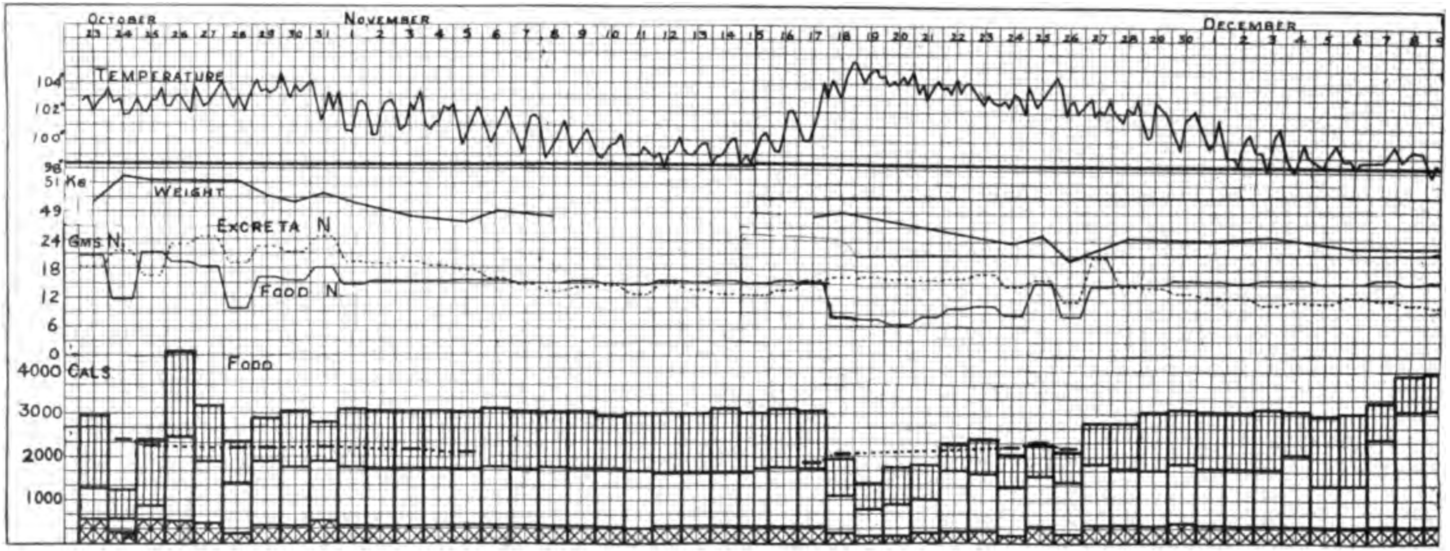

Chart 3.—Part 1

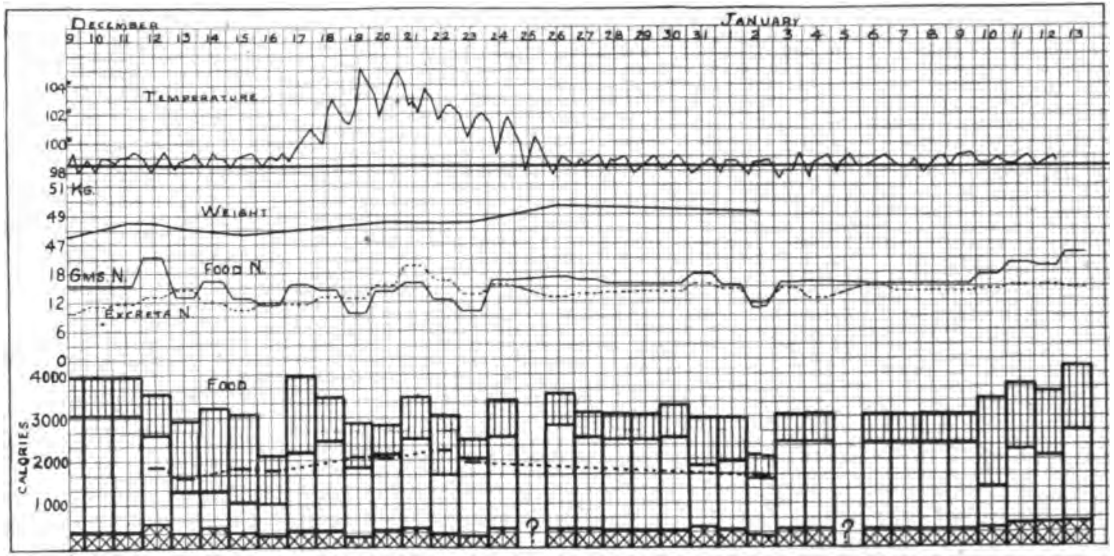

Chart 3.—Part 2

Chart 3.—Morris S.—Temperature, body weight. Food nitrogen, continuous line; excreta nitrogen, dotted line. At the base of the chart, columns representing total calories of food. Protein calories, crossed diagonals — fat calories, blank — carbohydrate calories, vertical lines. The dot-dash line represents the estimated heat production in calories for twenty-four hours. The dashes are placed on days of the observations in the calorimeter. Note that the calories of the food exceed the estimated heat production except for a period during the first relapse. Food was not measured on December 25th and January 5th.

him off with warm water, slides him from his bed to the weighing platform, makes up his bed and slides him back again. During the rest of the day he is seldom disturbed and he spends his time dozing, reading or talking with his neighbors. A few of the patients have been mildly irrational for a few days at a time and such occurrences have been noted in detail in the histories. Subsultus tendinum and jactitation have rarely been observed. On the other hand, there must be a reduction of the metabolism at night since the patients sleep soundly and are seldom disturbed. In a previous paper we have estimated that the bodily activity increases the metabolism during the whole day to an average of 10 per cent. above its basal metabolism. Since that time we have had the opportunity of making two observations on patients who were irrational and restless. November 3 Morris S. was in the calorimeter for three hours. During the first hour he was unusually quiet, during the second hour he was restless and tossed about the bed, during the third hour he was evidently irrational, tossed about and wrote three or four long notes which he held up to the calorimeter window to tell us about the animals that were biting him with their sharp teeth.

In spite of this unusual activity his metabolism during the three hour period was only 43 per cent. above the normal and was only 5 per cent. higher than during the quiet basal observation made two days later, when the temperature was lower. Edward B. on Nov. 10, 1914, was in the calorimeter with a temperature of 40.3 C., and during the second and third hours was restless and mildly irrational. His heat production was only 51 per cent. above the average normal. These two observations, which are fair samples of the severest symptoms observed in the typhoid patients presented in this paper, do not indicate any unusual degree of increase of heat production from the moderate activity. There may be an uneconomical expenditure of energy in typhoid in the performance of a certain task but even so the total expenditure is not great in these cases. It is hoped that at a later date the question of muscular efficiency in fever may be solved by having typhoid patients and normal controls do a stated amount of work on an ergometer while in the calorimeter.

A detailed consideration of all the factors is of importance when one attempts to draw conclusions from a discrepancy between the calculated intake and the calculated output. It is necessary to consider the possible errors in the various determinations and it is necessary to select somewhat arbitrary average percentages for the various factors. The measurement of the food intake is unusually accurate. Most of

the foods such as cereals, bread, sugars, egg white and egg yolk, butter and crackers vary but slightly from the samples analyzed. The other foods given, such as milk, cream, and dried apples are not subject to large enough variations to affect the results. Foods subject to significant variations are carefully avoided.

The methods of preparation and weighing have been described in another paper and they are believed to be accurate within 2 per cent. It is doubtful if this error combined with the error in the variation of the individual foods exceeds plus or minus 5 per cent. and there is no factor to throw the error on one side of the scale more often than on the other. The heat production of the patients as determined by the method of indirect calorimetry is not subject to an error of more than 1 or 2 per cent. on the average, although it is possible that some individual observations may show an error of 5 per cent. The collection of the twenty-four hour specimens of urine and the estimation of

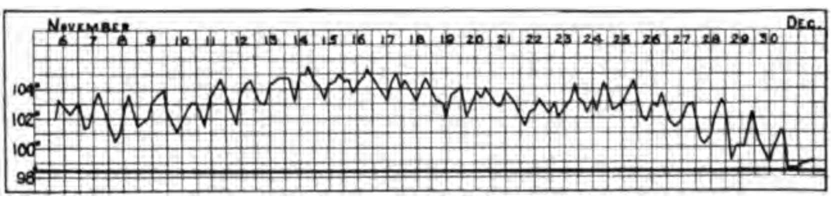

Chart 4.—Charles F. Temperature curve.

the nitrogen are so carefully controlled by duplicate analyses and checks in the collection of specimens and in the calculations that there is no chance for an error greater than 1 per cent. In the cases in which the feces were not analyzed the method of estimating the feces nitrogen as 10 per cent. of the food nitrogen gives a plus or minus error of less than half a gram a day while there is possibly as great an error in the fact that we do not take into account the nitrogen losses through the skin.

In order to estimate the caloric output of typhoid patients on whom respiration experiments were made, one can add to the basal metabolism on average 3 per cent. for the specific dynamic action of the food and 10 per cent. for muscular activity. We can, therefore, calculate with reasonable accuracy the heat production for the day by adding 13 per cent. to the figures obtained in the febrile basal experiments and 10 per cent. to the figures obtained in the experiments after food. In the cases in which several observations were made it seems fair to plot a smooth curve and consider that the heat production of the non-experi-

mental days was the same as on the days in which actual determinations were made.

If we look now at Table 4 and Charts 3, 6 and 8, it becomes evident that three of the patients reported in this paper and one reported in a previous paper[1] showed a distinct negative nitrogen balance when they were receiving considerably more calories than were sufficient to cover the calculated heat production. A glance at the food charts will show that the typhoid patients were given 12 to 16 grams of nitrogen a day and that the proportions of fat and carbohydrate were well balanced. The only criticism of the manner of feeding is that on the days of the basal determinations it was necessary for the patient to fast sixteen to twenty hours. One might expect a slight negative nitrogen balance at such times, but this should be offset by a positive balance the next day. As a matter of fact the negative balance is not much greater on the experi-

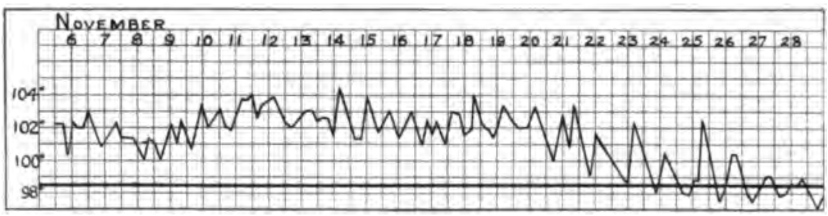

Chart 5.—Howard F. Temperature curve.

mental days. Moreover, as was pointed out in the previous paper, many patients who have not been the subject of respiration experiments have shown a persistent negative nitrogen balance on a diet much greater than the estimated heat production and have not come into nitrogen equilibrium until the theoretical requirement was exceeded by from 50 to 110 per cent.

In another place[1] when touching on this subject we referred to the possibility of a storage of fat while there was a negative nitrogen balance and loss of body weight. The body weight is notoriously a poor index of gain or loss of body tissue except in long periods of observation. The body changes its content of water so easily and so rapidly with changing diets and changing periods of the disease that it would be very easy to store 1 or 2 kilograms of fat without noticeable effect on the weight. We must remember that 1 kilogram of fat represents about 9,300 calories. Even without assuming a change in the water concentration of the body, it is possible to account for the storage of the excess calories. In the tables one can find several periods of almost con-

stant body weight when the patient was losing nitrogen. If we consider that for every 3 grams of nitrogen lost the patient loses about 100 grams of muscle tissue, it is possible to calculate the total muscle tissue lost. If this were replaced by fat the weight would remain constant and the storage of the excess calories could easily be accounted for. For example, Morris S. between October 23 and November 3 lost about 1,770 grams of muscle tissue, which could be replaced by enough fat to represent 15,900 calories.

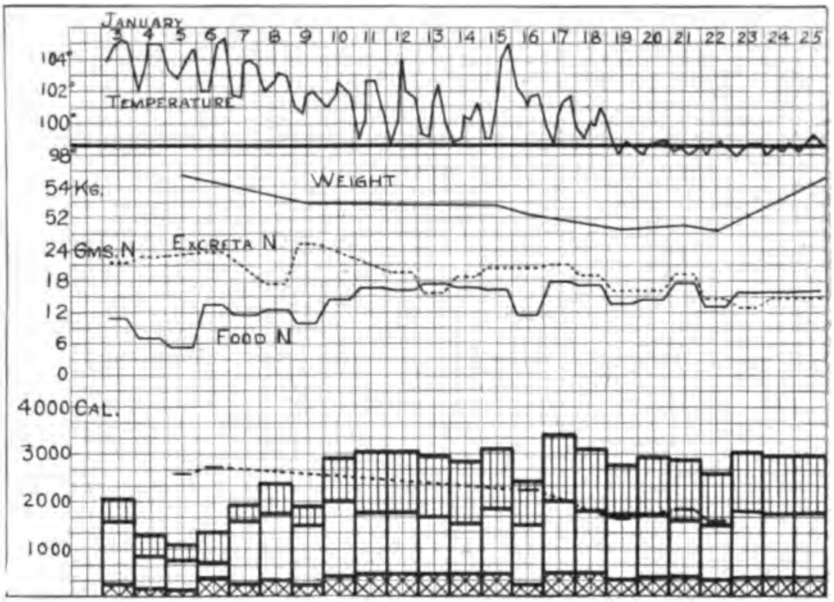

Chart 6.—Karl S. Temperature and body weight. Food nitrogen, continuous line; excreta nitrogen, dotted line. The columns at base represent calories in food. Protein calories crossed diagonals, fat calories blank, carbohydrate calories vertical lines. Dot-dash line represents the estimated heat production in calories for twenty-four hours, dashes being placed on the days of the calorimeter observations. Note the negative balance during the last days of the fever when the patient was receiving in food more calories than the estimated heat production.

In none of the cases were the protein and carbohydrate calories together sufficient to cover the heat production, so it is not necessary to assume the transformation of carbohydrate into fat, although we have shown that this is possible during fever in one patient[1] (Salvatore L.).

The Toxic Destruction of Protein.—The proof of the fact that typhoid patients show a negative nitrogen balance on a diet which furnishes more calories than the heat production, is perhaps the most

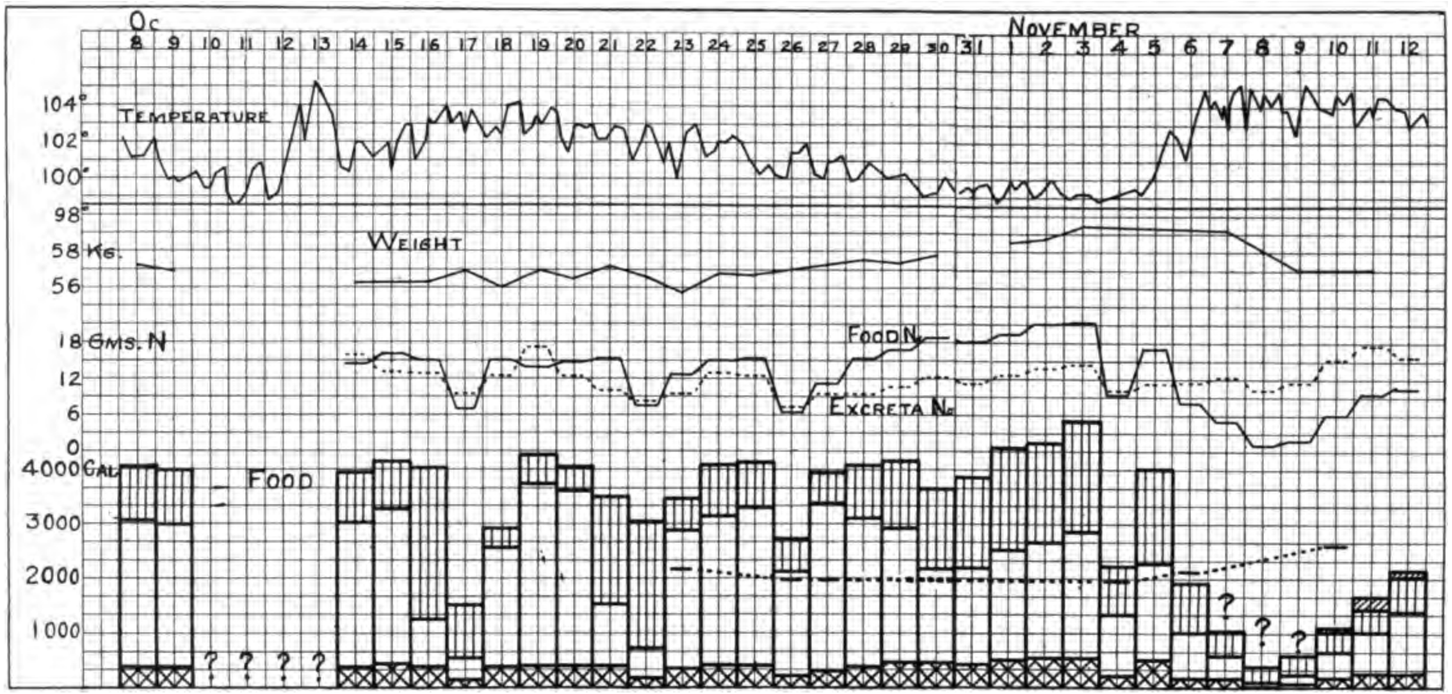

Chart 7.—Edward B. Temperature, body weight, food and excreta nitrogen. Food calories and dot-dash line representing estimated heat production. On November 7th, 8th and 9th, patient vomited, making measurement of food intake somewhat inaccurate. November 10th, 11th and 12th he received some alcohol calories.

important piece of evidence which has yet been presented in the discussion of the so-called toxic destruction of protein. Clinicians have long been aware of the large excretion of nitrogen in fever and have attributed it to an abnormal destruction of protein caused by the toxins of the disease. It is not necessary in this connection to review the older clinical work, since that is admirably presented in the standard discus-

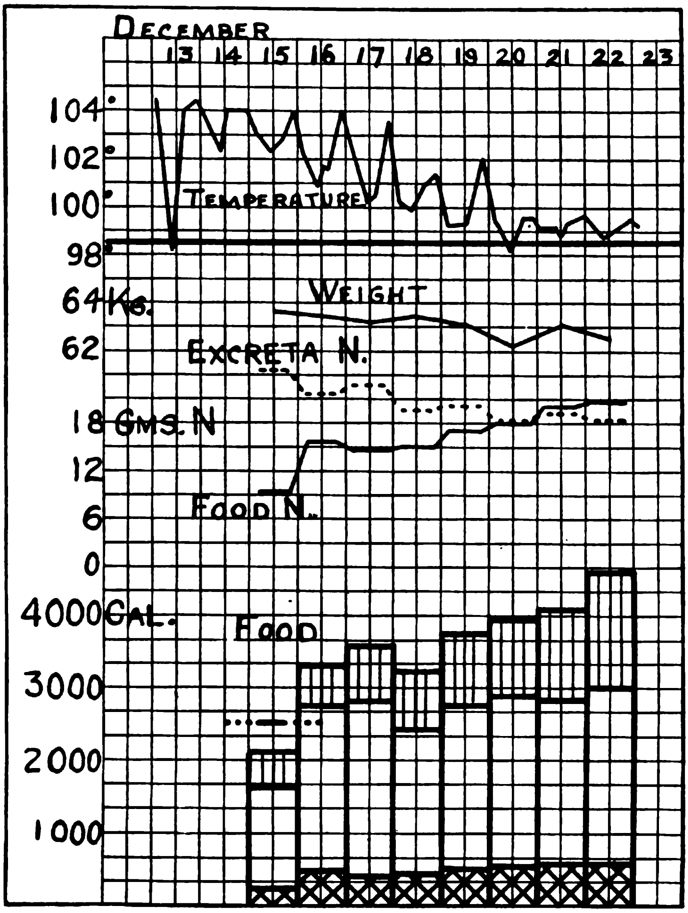

Chart 8.—John K. Temperature, body weight, food and excreta nitrogen. Food calories and dot-dash line showing estimated heat production.

sions of metabolism in fever. The results of the large number of investigations made on lower animals, while important, cannot with certainty be transferred to man.

The question of the toxic destruction of protein took on a new aspect when in 1909 Shaffer and Coleman[6] showed that it was possible

to obtain nitrogen balance in typhoid patients, even during the second and third weeks of the disease. This they accomplished only by making the total caloric value of the food very high, from 60 to 90 calories per kilogram, and the food nitrogen from 9 to 15 grams. In their discussion of the results they expressed the opinion that "....it is perhaps improbable that the total heat production reached the values represented by the larger amounts of food." This work proved that there was no toxic destruction in the sense of a nitrogen loss which could not be counterbalanced by the nitrogen intake.

The question of the average heat production of typhoid patients was fully discussed in last year's paper[1] and attention was drawn to the fact that typhoid patients did not come into nitrogen equilibrium until their theoretical caloric requirement was exceeded by from 50 to 110 per cent. Grafe[10] in 1911 had shown that his typhoid patients when studied in a respiration chamber, ten to sixteen hours after their last meal, derived about 10 to 20 per cent. of their calories from protein, a percentage usually found in normal men. From this Grafe concluded that he had shown that the protein metabolism in fever was not abnormal. The percentage of calories derived from protein on the first eighteen hours after food ingestion depends largely on the previous level of the protein metabolism. Normal individuals who have been taking 15 to 19 grams of nitrogen a day will naturally derive about 15 to 20 per cent. of their calories from protein as is shown in Paper 4 of this series. Normal individuals who have been maintaining themselves in nitrogen balance on 4 to 5 grams a day will derive only 5 per cent. of their calories from protein. The comparison should have been made between normal men and typhoid patients while both were on their nitrogen minima. This will be shown later in a discussion of Kocher's work.

Rolland[11] working under Grafe's direction brought several fever patients into nitrogen balance by means of a caloric intake which she believed to be equal to the heat production as estimated from the averages of other patients. Respiration experiments were not made on the patients themselves. Our reasons for believing that the food intake was above the requirement have been set forth in another place[1] (p. 38).

Recent work from Friedrich Müller's clinic has thrown important light on the subject. Graham and Poulton[12] established themselves

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10. Grafe E.: Untersuchungen über den Stoff- und Kraftwechsel im Fieber, Deutsch. Arch. f. klin. Med., 1911, ci, 209.

11. Rolland, Anne: Zur Frage des toxogenen Eiweisszerfalls im Fieber des Menschens, Deutsch. Arch. f. klin. Med., 1912, cvii, 440.

12. Graham and Poulton: Influence of Temperature on Protein Metabolism, Quart. Jour. Med., 1912, vi, 82.

on a minimal nitrogen elimination of 4 to 5 grams a day and found no increase in the elimination when they raised their temperatures to about 40 C. by means of a steam bath. Kocher[13] in two normal subjects established a nitrogen minimum at a similar level and found no increase when he raised the heat production by means of a 60 kilometer walk. All of these experiments were made on a caloric intake calculated to cover the requirement. They indicate that rise in temperature alone or increase in heat production alone will not cause an increased protein metabolism, at least when applied for a portion of one day. Kocher then attempted by means of a diet amply sufficient to cover the calculated requirement to bring down the nitrogen elimination of fever patients to the low level obtained in normal men. This he found to be impossible until the active stage of the disease was passed. Grafe[14] in a recent paper has criticized these experiments.

To all of the patients in Table 4 food was given which had an energy content much greater than the amount required by the patients as measured directly when they were in the calorimeter. Although the protein content of the diet, as represented by an intake of 15 grams of nitrogen, was ample to establish nitrogen equilibrium had the diet been given to normal men, it did not accomplish this in typhoid fever. It is difficult to see in this anything except the proof that there is an abnormal destruction of protein in typhoid fever. In some cases the protein destruction continued several days after the temperature had reached a low level. It is impossible to escape the conclusion that the destruction of protein is caused by the toxins of the disease.

SUMMARY AND CONCLUSIONS

The heat production of typhoid patients has been measured by the methods of direct and indirect calorimetry in a series of sixty-one experiments. The two methods agreed closely, the total divergence being 2.2 per cent. and the average divergence in the individual experiments being 5 per cent. This and the entire absence of abnormal respiratory quotients indicate that in typhoid fever protein, fat and carbohydrate are oxidized to the same or approximately the same end products as in health, and in their oxidation give off the standard

13. Kocher, Rudolph A.: Ueber die Grosse des Eiweisszerfalls bei Fieber und bei Arbeitsleitstung, Deutsch. Arch. f. klin. Med., 1914, cxv, 82.

14. Grafe, E.: Zur Genese des Eiweisszerfalls im Fieber, Deutsch. Arch. f. klin. Med., 1914, cvi, 328.

Subject Date Weight	Period	End of Period	Carbon-dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calo-rimetry, Cal.	Heat Elimi-nated, Cal.	Direct Calo-rimetry (Rectal Temp.) Cal.	Rectal Temp. C.
Morris S. ...... Oct. 24, '18 51.50 kg.	Prelim.	11:35	.....	.....	..	.....	.....	.....	.....	.....	39.86
	1	12:35	30.06	30.02	.73	47.84	0.713	97.69	88.41	84.28	39.95
	2	1:35	27.82	26.18	.77	46.72	0.713	85.89	84.68	81.00	39.89
	3	2:35	26.20	24.04	.79	39.48	0.713	79.28	74.68	85.72	40.17
Morris S. ...... Oct. 25, '18 51.22 kg.	Prelim.	11:00	.....	.....	..	.....	.....	.....	.....	.....	39.21
	1	12:00	29.65	26.82	.80	42.10	0.671	88.95	78.03	90.06	39.49
	2	1:00	28.63	25.87	.81	39.10	0.671	85.77	80.11	88.09	39.69
	3	2:00	31.75	25.46	.91	42.82	0.671	86.62	90.07	78.55	39.49
Morris S. ...... Oct. 28, '18 51.50 kg.	Prelim.	11:10	.....	.....	..	.....	.....	.....	.....	.....	39.62
	1	12:10	34.12	28.35	.88	43.31	0.732	95.71	92.00	75.58	39.27
	2	1:10	32.64	24.82	.96	42.41	0.732	85.31	94.67	76.33	38.87
	3	2:10	30.25	22.89	.96	39.40	0.732	78.60	86.73	84.65	38.81
	4	3:10	29.98	24.33	.90	34.39	0.732	82.34	78.47	98.97	39.20
	5	4:10	28.38	22.05	.94	31.75	0.732	74.59	74.35	90.84	39.65
Morris S. ...... Oct. 29, '18 49.86 kg.	Prelim.	11:10	.....	.....	..	.....	.....	.....	.....	.....	39.68
	1	12:10	26.75	23.77	.82	33.11	0.658	79.00	81.19	76.49	39.50
	2	1:10	27.49	25.95	.77	34.03	0.658	85.28	84.48	85.73	39.54
Morris S. ...... Oct. 31, '18 50.28 kg.	Prelim.	11:00	.....	.....	..	.....	.....	.....	.....	.....	39.06
	1	12:00	28.95	25.45	.83	32.13	1.058	84.11	74.09	58.27	38.94
	2	1:00	29.69	24.17	.89	36.41	1.058	81.15	79.19	79.96	39.08
	3	2:00	29.57	26.58	.80	36.76	1.058	87.50	77.70	87.18	39.43
Morris S. ...... Nov. 3, '18 48.53 kg.	Prelim.	10:30	.....	.....	..	.....	.....	.....	.....	.....	38.63
	1	11:30	24.91	20.42	.89	28.58	0.499	69.20	56.44	72.99	39.05
	2	12:30	28.70	26.23	.80	33.10	0.499	83.77	74.39	77.80	39.15
	3	1:30	27.53	27.90	.72	42.11	0.499	90.92	86.25	71.74	38.81
Morris S. ...... Nov. 5, '18 48.45 kg.	Prelim.	11:20	.....	.....	..	.....	.....	.....	.....	.....	38.08
	1	12:20	25.42	23.10	.80	29.99	0.491	76.70	77.98	81.84	38.19
	2	1:20	26.42	23.05	.83	38.62	0.491	77.19	74.75	67.00	38.01
	3	2:20	25.60	23.65	.79	39.13	0.491	78.29	72.89	75.84	38.10
Morris S. ...... Nov. 17, '18 47.99 kg.	Prelim.	11:10	.....	.....	..	.....	.....	.....	.....	.....	38.48
	1	12:10	21.90	19.01	.84	24.39	0.336	63.87	57.98	62.77	38.61
	2	1:10	23.58	20.82	.82	24.44	0.336	69.76	60.70	69.71	38.82
	3	2:10	23.79	22.28	.78	26.06	0.336	73.79	66.08	72.85	39.00
Morris S. ...... Nov. 18, '18 48.77 kg.	Prelim.	11:00	.....	.....	..	.....	.....	.....	.....	.....	39.72
	1	12:00	24.40	22.01	.81	26.55	0.567	73.01	67.36	64.94	39.67
	2	1:00	26.37	21.38	.90	28.15	0.567	72.56	71.65	82.60	39.98
	3	2:00	25.91	23.57	.80	28.88	0.567	78.11	72.05	77.47	40.15
Morris S. ...... Nov. 24, '18 46.69 kg.	Prelim.	11:13	.....	.....	..	.....	.....	.....	.....	.....	39.54
	1	12:13	29.17	25.27	.78	29.24	0.514	83.56	67.50	68.12	39.59
	2	1:13	26.91	24.54	.75	32.68	0.514	85.26	75.16	64.72	39.33
	3	2:13	26.41	25.48	.75	35.00	0.514	83.64	80.48	73.52	39.16

Surface Temp., C.	Average Pulse	Work Adder., Cm.	Non-Protein, R. Q.	Per Cent. Calories from			Calories Per Hour		Remarks
				Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M.	
.....	96(?)	36.0	.71	24	75	1	1.90	57.33	Basal.
.....	96	21.0	.77	28	58	14	1.67	50.40	
.....	105	17.0	.79	31	49	20	1.54	46.58	
.....	101	30.0+	.80	20	54	26	1.74	52.86	9:30-10:00 a. m., protein meal. 9.0 gm. N.
.....	96	21.5	.81	21	52	27	1.68	50.48	
.....	105	18.0++	.94	21	17	62	1.69	50.98	
.....	119	35.0	.90	20	29	51	1.88	66.70	At 10:22, 115 gm. com. glucose = 100 gm. dextrose. Asleep from 3-3:40.
.....	118	25.0+5?	1.01	23	..	77	1.68	50.54	
.....	108	30.5	1.02	25	..	75	1.55	46.56	
.....	108	18.0	.98	24	19	57	1.62	48.78	
.....	107	9.0	.99	26	3	71	1.47	44.19	
.....	105	24.0	.82	22	47	31	1.58	47.17	Basal.
.....	106	17.5	.76	20	65	15	1.70	50.91	
.....	101	10.0 (?)	.84	33	36	31	1.68	50.16	8:40-9:20, protein meal; 10.3 gm. N.
.....	102	11.2+	.95	35	12	53	1.62	48.39	
.....	98	9.5	.81	32	44	24	1.74	52.18	
.....	106	11.7	.91	19	25	56	1.42	42.09	Basal. 1st. hr. quiet, 2d. hr. restless, 3d. hr. restless; wrote 3 or 4 notes.
.....	111	32.0	.79	16	59	25	1.71	50.96	
.....	106	8.0+	.70	15	85	..	1.86	55.30	
.....	98	5.5	.80	17	56	27	1.58	46.89	Basal.
.....	109	8.0	.84	17	45	38	1.59	47.18	
.....	112	8.0	.78	17	61	22	1.62	47.86	
37.29									
37.52	100	11.0	.84	14	45	41	1.33	39.28	Basal.
37.83	113	6.8	.83	13	51	36	1.45	42.90	
37.94	112	3.0	.77	12	68	20	1.54	45.38	
38.89									
38.98	114	0.3	.81	21	52	27	1.50	44.44	Basal.
39.27	117	14.7	.92	21	20	59	1.49	44.16	
39.16	124	13.7	.80	19	55	26	1.60	47.54	
.....	...	12.0	.78	16	64	20	1.77	52.82	Basal.
.....	122	0.0	.74	16	73	11	1.81	53.39	
.....	126	0.5	.74	16	73	11	1.78	52.37	

Subject Date Weight	Period	End of Period	Carbon-dioxid, Gm.	Oxygen. Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.	Direct Calorimetry (Rectal Temp.) Cal.	Rectal Temp. C.
Morris S. ...... Nov. 25, '13 47.24 kg.	Prelim.	11:20	.....	.....	..	.....	.....	.....	.....	.....	39.40
	1	12:20	28.17	24.45	.84	29.86	0.618	81.79	71.86	66.66	39.30
	2	1:20	30.38	26.92	.82	47.61	0.618	89.78	91.51	78.22	38.97
	3	2:20	29.26	27.94	.78	48.78	0.618	89.93	88.95	95.35	39.13
Morris S. ...... Nov. 26, '13 46.11 kg.	Prelim.	10:50	.....	.....	..	.....	.....	.....	.....	.....	39.61
	1	11:50	26.29	24.80	.77	27.88	0.329	82.10	69.06	52.60	39.19
	2	12:50	25.68	24.64	.76	34.79	0.329	81.28	79.19	71.14	38.99
	3	1:50	25.70	24.85	.75	42.13	0.329	81.84	88.38	79.59	38.77
Morris S. ...... Dec. 12, '13 48.61 kg.	Prelim.	10:56	.....	.....	..	.....	.....	.....	.....	.....	37.01
	1	11:56	23.45	20.22	.84	18.48	0.272	68.20	61.73	58.71	36.82
	2	12:56	23.88	20.96	.83	21.26	0.272	70.44	64.58	69.48	36.95
	3	1:56	24.99	21.42	.85	24.01	0.272	72.36	66.64	69.52	37.03
Morris S. ...... Dec. 13, '13 48.07 kg.	Prelim.	10:36	.....	.....	..	.....	.....	.....	.....	.....	37.07
	1	11:36	18.99	16.89	.82	18.84	0.323	56.39	58.07	50.93	36.90
	2	12:36	20.10	17.29	.85	19.31	0.323	58.16	58.63	63.06	37.02
	3	1:36	20.76	18.90	.80	20.26	0.323	62.88	61.95	63.59	37.07
Morris S. ...... Dec. 15, '13 48.17 kg.	Prelim.	10:52	.....	.....	..	.....	.....	.....	.....	.....	37.30
	1	11:52	24.51	18.29	.98	18.41	0.384	63.45	58.74	47.60	37.03
	2	12:52	26.76	18.98	1.03	20.90	0.384	66.42	63.52	64.97	37.10
	3	1:52	26.83	18.82	1.04	22.07	0.384	65.97	64.19	67.97	37.23
Morris S. ...... Dec. 16, '13 47.86 kg.	Prelim.	11:06	.....	.....	..	.....	.....	.....	.....	.....	37.32
	1	12:06	22.51	17.81	.92	20.83	0.299	61.10	63.36	61.62	37.30
	2	1:06	21.91	18.33	.87	21.42	0.299	62.12	62.76	63.36	37.33
	3	2:06	22.37	19.33	.84	21.70	0.299	65.06	63.87	60.35	37.25
Morris S. ...... Dec. 19, '13 48.74 kg.	Prelim.	11:10	.....	.....	..	.....	.....	.....	.....	.....	39.19
	1	12:10	27.88	21.99	.91	22.55	0.493	74.94	70.40	67.95	39.14
	2	1:10	30.04	22.70	.96	25.64	0.493	78.51	75.00	84.00	39.41
	3	2:10	29.47	23.51	.91	27.26	0.493	80.82	74.21	87.13	39.75
Morris S. ...... Dec. 20, '13 48.52 kg.	Prelim.	10:40	.....	.....	.	.....	.....	.....	.....	.....	39.20
	1	11:40	23.69	22.51	.77	23.81	0.547	73.93	67.11	76.36	39.53
	2	12:40	25.60	23.42	.80	25.60	0.547	77.57	70.95	78.45	39.76
	3	1:40	25.51	23.84	.78	27.47	0.547	78.68	72.88	72.56	39.77
Morris S. ...... Dec. 22, '13 48.87 kg.	Prelim.	11:16	.....	.....	..	.....	.....	.....	.....	.....	38.65
	1	12:36	37.28	28.77	.94	37.28	0.705	98.85	97.57	112.89	39.05
	2	1:36	28.84	22.32	.94	28.28	0.529	76.65	73.08	88.65	39.47
	3	2:36	28.86	22.21	.95	29.24	0.529	76.39	74.60	78.88	39.59
Morris S. ...... Dec. 23, '13 48.60 kg.	Prelim.	11:06	.....	.....	..	.....	.....	.....	.....	.....	38.04
	1	12:06	23.51	21.45	.80	25.82	0.428	71.21	68.75	73.19	38.16
	2	1:06	23.94	21.92	.80	25.39	0.428	72.73	70.84	80.86	38.46
	3	2:06	24.85	22.79	.78	25.38	0.428	75.82	69.85	76.84	38.66
Morris S. ...... Jan. 2, '14 49.26 kg.	Prelim.	11:16	.....	.....	..	.....	.....	.....	.....	.....	36.97
	1	12:16	19.10	16.62	.84	19.75	0.386	55.68	58.53	52.15	36.85
	2	1:16	19.27	17.07	.82	20.20	0.386	56.94	57.89	64.98	37.06
	3	2:16	19.80	18.33	.78	22.05	0.386	60.77	61.54	60.88	37.07

Surface Temp., C.	Average Pulse	Work Adder., Gm.	Non-Protein, R. Q.	Per Cent. Calories from			Calories Per Hour		Remarks
				Protein	Fat	Carbohyd.	Per Kg	Per Sq. M.	
38.37									
38.66	112	18.5	.85	20	42	38	1.72	50.88	9.35:10:15, protein meal; 8.7 gm. N. Began to sweat at end of second hour.
38.12	122	12.2	.88	18	49	33	1.89	55.80	
37.76	119	9.5	.78	18	62	20	1.90	55.89	
38.87									
38.59	112	5.5	.77	11	70	19	1.79	51.83	Basal. Patient restless in second period.
38.18	119	11.0+	.75	11	75	14	1.77	51.81	
37.58	123	12.0	.75	11	77	12	1.78	51.67	
35.60									
35.52	91	8.8	.85	11	46	43	1.40	41.59	9:08-9:30, protein meal; 10.6 gm. N.
35.69	94	18.6	.88	10	51	39	1.45	42.95	
35.73	98	14.5	.85	10	45	45	1.49	44.12	
35.82									
35.64	74	9.0	.82	15	52	33	1.17	34.64	Basal. Asleep in first period.
35.82	88	9.2	.85	15	43	42	1.21	35.78	
35.96	87	7.5	.80	14	59	27	1.31	38.62	
35.98									
35.54	88	6.0	1.01	16	..	84	1.32	38.95	At 10:13, 115 gm. commercial glucose.
35.72	102	5.1	1.07	15	..	85	1.38	40.77	
35.75	100	1.2	1.09	15	..	85	1.37	40.50	
35.99									
35.93	84	5.7	.94	13	18	69	1.28	37.65	Basal.
35.95	87	2.5	.88	13	35	52	1.30	38.27	
36.00	93	7.0	.85	12	46	42	1.36	40.10	
37.52									
37.29	105	0.3	.93	17	20	63	1.54	45.64	At 10:26, 115 gm. commercial glucose.
37.64	121	7.3	1.00	17	1	82	1.61	47.81	
37.71	121	2.0	.94	16	19	65	1.65	48.92	
37.49									
37.59	108	1.6	.76	20	67	13	1.55	45.13	Basal.
37.87	114	8.1	.79	19	57	24	1.63	47.86	
37.91	117	2.2	.77	18	64	18	1.65	48.00	
36.85									
37.44	109	9.2	.98	19	6	75	1.52	45.07	At 10:24, 115 gm. commercial glucose. First period 1 hr. 20 min. because patient moved at end of hour.
37.67	120	6.5	.97	18	8	74	1.57	46.61	
37.71	120	1.2	.98	18	6	76	1.57	46.44	
36.64									
36.02	99	1.2	.80	16	58	26	1.46	43.42	Basal.
36.80	100	9.2	.79	16	59	25	1.50	44.35	
37.07	105	4.0	.77	15	66	19	1.55	45.93	
35.49									
35.57	69	8.8	.84	18	44	38	1.13	33.63	Basal.
35.57	76	1.6	.83	18	49	33	1.15	34.43	
35.71	79	4.6	.78	17	57	26	1.23	36.74	

Subject Date Weight	Period	End of Period	Carbon-dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calo-rimetry, Cal.	Heat Elimi-nated, Cal.	Direct Calo-rimetry (Rectal Temp.) Cal.	Rectal Temp. C.
Morris S. ...... Jan. 27, '14 57.50 kg.	Prelim.	11:45	.....	.....	..	.....	.....	.....	.....	.....	37.06
	1	12:45	19.39	17.28	.82	21.44	0.365	57.63	69.67	56.44	36.79
	2	1:45	22.28	19.73	.82	21.96	0.365	65.98	71.20	73.22	36.90
	3	2:45	22.21	19.73	.82	22.74	0.365	65.94	70.02	72.00	36.97
Morris S. ...... Dec. 17, '14 61.21 kg.	Prelim.	11:27	.....	.....	..	.....	.....	.....	.....	.....	36.89
	1	12:27	21.46	19.30	.81	25.58	0.381	64.27	70.65	64.61	36.70
	2	1:27	23.25	21.17	.80	27.85	0.381	70.42	72.99	70.69	36.79
	3	2:27	23.02	20.52	.82	27.74	0.381	68.53	72.30	68.84	36.81
Morris S. ...... Dec. 18, '14 62.81 kg.	Prelim.	11:00	.....	.....	..	.....	.....	.....	.....	.....	37.02
	1	12:00	27.56	22.40	.90	31.97	0.409	76.31	77.07	71.53	36.92
	2	1:00	29.29	24.39	.87	34.09	1.101	81.43	84.04	82.67	36.94
	3	2:00	23.14	19.14	.88	29.33	1.101	63.50	76.85	73.79	36.89
	4	3:00	25.29	21.01	.88	31.79	1.101	69.82	78.61	74.47	36.85
Charles F. .... Nov. 10, '13 57.78 kg.	Prelim.	11:10	.....	.....	..	.....	.....	.....	.....	.....	38.94
	1	12:10	26.83	24.23	.81	26.28	0.514	80.56	66.11	79.70	39.21
	2	1:10	27.37	25.08	.79	28.78	0.514	83.17	71.87	73.83	39.26
	3	2:10	27.91	25.99	.78	43.30	0.514	85.95	88.09	77.90	39.05
Charles F. .... Nov. 11, '13 58.22 kg.	Prelim.	11:20	.....	.....	..	.....	.....	.....	.....	.....	38.82
	1	12:20	28.97	24.58	.86	25.84	0.930	82.08	67.32	78.06	39.05
	2	1:20	30.21	26.74	.82	31.12	0.930	88.58	77.70	86.96	39.25
	3	2:20	31.40	27.66	.83	31.13	0.930	91.78	82.04	99.99	39.63
Charles F. .... Nov. 14, '13 57.94 kg.	Prelim.	11:10	.....	.....	..	.....	.....	.....	.....	.....	39.62
	1	12.10	32.69	26.60	.89	32.29	0.813	89.98	83.73	83.31	39.62
	2	1:10	31.92	25.64	.91	32.26	0.813	87.23	81.28	68.87	39.37
	3	2:10	32.24	26.33	.89	32.95	0.813	88.98	89.47	91.35	39.49
Charles F. .... Nov. 15, '13 57.03 kg.	Prelim.	11:16	.....	.....	..	.....	.....	.....	.....	.....	39.77
	1	12:16	28.26	26.44	.78	28.84	0.657	87.09	75.09	82.25	39.93
	2	1:16	28.23	26.98	.79	32.35	0.657	86.12	86.12	74.34	39.88
Charles F. .... Nov. 29, '13 50.36 kg.	Prelim.	11:26	.....	.....	..	.....	.....	.....	.....	.....	36.71
	1	12:26	21.39	18.31	.85	29.25	0.483	61.69	61.79	59.74	36.67
	2	1:26	22.05	20.15	.80	28.24	0.483	67.01	63.78	75.00	37.00
	3	2:26	21.99	19.44	.82	27.10	0.483	65.08	63.75	72.92	37.25
Charles F. .... Dec. 8, '13 50.99 kg.	Prelim.	11:10	.....	.....	..	.....	.....	.....	.....	.....	36.90
	1	12:10	25.97	19.63	.96	21.83	0.817	66.98	62.72	52.64	36.67
	2	1:10	26.73	21.61	.90	25.30	0.817	72.92	70.29	75.47	36.85
	3	2:10	25.97	21.12	.90	29.04	0.817	71.18	74.23	76.85	36.95
Charles F. .... Dec. 9, '13 50.38 kg.	Prelim.	11:06	.....	.....	..	.....	.....	.....	.....	.....	36.78
	1	12:06	22.60	18.05	.91	19.36	0.380	61.66	58.80	55.10	36.70
	2	1:06	22.10	17.29	.93	22.22	0.380	59.30	64.40	69.90	36.87
	3	2:06	21.98	17.63	.91	22.36	0.380	60.15	61.83	61.55	36.88
Charles F. .... Dec. 10, '13 51.09 kg.	Prelim.	11:10	.....	.....	..	.....	.....	.....	.....	.....	36.89
	1	12:10	26.98	20.24	.97	22.40	0.362	70.28	62.46	58.29	36.80
	2	1:10	27.70	19.45	1.04	24.37	0.362	68.24	68.32	64.48	36.76
	3	2:10	25.68	18.90	.99	28.76	0.362	65.28	72.63	60.44	36.50

Surface Temp., C.	Average Pulse	Work Adder., Cm.	Non-Protein, R. Q.	Per Cent. Calories from			Calories Per Hour		Remarks
				Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M.	
35.61									
35.11	60	0.5	.82	17	51	32	1.00	31.29	Basal.
35.15	71	5.6	.82	15	51	34	1.15	35.82	
35.37	68	5.2	.82	15	52	33	1.15	35.80	
.....	62	4.0	.81	16	55	29	1.05	33.61	Basal.
.....	65	6.0	.80	14	58	28	1.15	36.88	
.....	62	5.0	.82	15	52	33	1.12	35.08	
.....	..	5.0	.91	14	21	65	1.22	39.23	At 8:40-9:40 a. m., protein meal; 9.6 gm. N.
.....	74	6.0	.92	36	17	47	1.30	41.87	
.....	70	6.0	.95	46	9	45	1.01	32.65	
.....	62	6.0	.93	42	14	44	1.11	35.90	
.....	76	3.5	.81	17	55	28	1.40	43.81	Basal.
.....	76	2.0	.79	16	60	24	1.44	45.23	
.....	82	9.0	.78	16	64	20	1.49	46.74	
37.69									
38.24	77	3.5	.88	30	28	42	1.41	44.34	9:10-10:10, protein meal; Nitrogen 6.6 gm.
38.25	86	13.0	.83	28	42	30	1.53	47.88	
38.34	84	4.0	.83	27	41	32	1.57	49.61	
38.79									
38.90	97	15.0	.93	24	19	57	1.56	48.80	At 10:21 a. m., 115 gm commercial glucose.
38.68	98	8.3	.94	25	15	60	1.52	47.81	
38.79	96	25.0	.92	24	21	55	1.55	48.25	
38.92									
39.10	90	17.0	.77	20	63	17	1.53	47.75	Basal.
39.04	88	15.5	.78	20	59	21	1.51	47.22	
.....	80	13.2	.86	21	37	42	1.23	36.81	Basal.
.....	86(?)	16.5	.79	20	56	24	1.33	39.98	
.....	84	18.8	.83	20	47	33	1.30	38.83	
36.24									
36.54	74	36.6	1.05	32	..	68	1.31	39.54	9:03-9:45, protein meal; 10.5 gm. N. Work adder too high on account of rapid changes in barometer.
36.16	72	20.3	.94	30	13	57	1.43	43.05	
36.37	84(92)	15.0	.94	30	15	55	1.40	41.99	
.....	75	22.3	.93	16	19	65	1.23	36.72	Basal.
.....	76	23.0	.96	17	12	71	1.18	35.32	
.....	84	9.7	.93	17	20	63	1.20	35.83	
.....	73	10.0	1.00	14	..	86	1.33	41.46	At 10:22, 115 gm. commercial glucose.
.....	87	23.5+2?	1.06	14	..	86	1.34	40.26	
.....	81	33.0+2?	1.02	15	..	85	1.29	38.81	

Subject Date Weight	Period	End of Period	Carbon-dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.	Direct Calorimetry (Rectal Temp.) Cal.	Rectal Temp. C.
Charles F. .... Dec. 26, '13 55.87 kg.	Prelim.	11:12	.....	.....	..	.....	.....	.....	.....	.....	36.84
	1	12:12	23.75	19.16	.90	26.72	0.275	65.56	75.47	75.27	36.90
	2	1:12	21.98	18.86	.85	25.23	0.275	63.65	69.83	67.08	36.86
	3	2:12	22.11	20.10	.80	25.14	0.275	67.08	70.63	69.23	36.85
Charles F. .... Dec. 31, '13 55.98 kg.	Prelim.	1:40	.....	.....	..	.....	.....	.....	.....	.....	37.08
	1	2:40	21.85	19.82	.80	22.56	0.403	65.85	66.09	59.70	36.95
	2	3:40	22.81	21.14	.78	26.98	0.403	69.98	69.09	68.75	36.95
Howard F. .... Nov. 7, '13 35.47 kg.	Prelim.	11:16	.....	.....	..	.....	.....	.....	.....	.....	39.74
	1	12:16	22.09	20.58	.78	22.79	.....	68.25	57.28	56.71	39.73
	2	1:16	21.02	19.75	.77	24.24	.....	65.53	64.17	63.90	39.73
	3	2:16	20.86	.....	..	24.06	.....	65.03 ?	64.99	60.30	39.58
Howard F. .... Nov. 12, '13 34.98 kg.	Prelim.	11:24	.....	.....	..	.....	.....	.....	.....	.....	39.64
	1	12:24	22.06	19.37	.83	20.58	0.612	64.40	58.89	61.38	39.74
	2	1:24	23.23	20.40	.83	23.38	0.612	67.88	63.72	65.61	39.89
	3	2:24	22.55	21.27	.77	23.60	0.612	69.78	68.49	70.09	40.15
Howard F. .... Nov. 13, '13 34.19 kg.	Prelim.	11:00	.....	.....	..	.....	.....	.....	.....	.....	39.76
	1	12:00	19.45	17.76	.80	22.80	0.436	58.81	57.80	59.64	39.84
	2	1:00	19.64	18.48	.77	22.62	0.436	60.86	58.19	57.19	39.82
	3	2:00	20.20	19.24	.76	23.66	0.436	63.22	63.74	62.17	39.78
Howard F. .... Nov. 20, '13 32.54 kg.	Prelim.	11:30	.....	.....	..	.....	.....	.....	.....	.....	39.31
	1	12:30	18.43	17.26	.78	27.43	0.354	56.98	55.72	55.87	39.33
	2	1:30	18.27	17.42	.76	27.31	0.354	57.30	63.70	58.16	39.14
	3	2:30	17.96	17.42	.75	25.62	0.354	57.10	59.75	58.97	38.94
Howard F. .... Dec. 1, '13 32.93 kg.	Prelim.	11:06	.....	.....	..	.....	.....	.....	.....	.....	37.03
	1	12:06	19.35	14.58	.97	18.80	0.292	50.50	45.34	42.26	36.93
	2	1:06	39.56	29.26	.98	37.03	0.292	101.68	46.88	97.14	36.96
	3	2:06							50.17		36.97
Howard F. .... Dec. 2, '13 33.06 kg.	Prelim.	11:12	.....	.....	..	.....	.....	.....	.....	.....	36.84
	1	12:12	15.46	12.42	.91	17.57	0.234	42.40	44.03	42.30	36.79
	2	1:12	18.09	13.48	.98	18.64	0.234	46.86	50.53	52.20	36.93
Howard F. .... Dec. 5, '13 34.74 kg.	Prelim.	11:06	.....	.....	..	.....	.....	.....	.....	.....	37.07
	1	12:06	22.13	17.23	.93	21.01	0.614	58.85	55.03	51.80	36.97
	2	1:06	24.24	17.61	1.00	21.99	0.614	60.75	61.84	64.82	37.17
	3	2:06	24.72	19.43	.93	23.61	0.614	66.21	64.12	65.52	37.25
Howard F. .... Dec. 6, '13 33.78 kg.	Prelim.	10:56	.....	.....	..	.....	.....	.....	.....	.....	37.02
	1	11:56	18.20	13.44	.98	17.44	0.267	46.71	47.83	46.67	36.99
	2	12:56	19.17	14.84	.94	18.30	0.267	51.14	51.37	51.43	37.06
Howard F. .... Dec. 18, '13 37.17 kg.	Prelim.	11:06	.....	.....	..	.....	.....	.....	.....	.....	37.11
	1	12:06	19.11	16.10	.86	18.73	0.314	54.38	53.61	52.94	37.10
	2	1:06	21.42	18.19	.86	20.94	0.314	61.42	58.80	63.36	37.29
	3	2:06	20.93	18.62	.81	23.84	0.314	62.26	65.14	63.04	37.25

Surface Temp., C.	Average Pulse	Work Adder., Cm.	Non-Protein, R. Q.	Per Cent. Calories from Protein	Per Cent. Calories from Fat	Per Cent. Calories from Carbohyd.	Calories Per Hour Per Kg.	Calories Per Hour Per Sq. M.	Remarks
36.02									
36.09	76	23.2	.92	11	26	63	1.18	36.44	Basal
36.38	..	18.8	.85	11	44	45	1.14	35.38	
35.74	..	10.2	.50	11	61	28	1.20	37.26	
36.90									
35.98	78	4.0	.80	16	57	27	1.18	36.38	Basal.
36.68	81	....	.78	15	64	21	1.25	38.66	
.....	100	10.0	....	..	..	..	1.91	51.85	Basal. Urine not obtained; O_2 lost in third period.
.....	103	6.0	....	..	..	..	1.83	49.81	
.....	106	2.0	....	..	..	..	1.83(?)	48.98(?)	
39.01									
39.18	105	2.5	.84	25	41	34	1.84	48.90	9:10-9:40, protein meal; 6.5 gm. N. Asleep most of first period.
39.30	104	9.5	.84	24	42	34	1.94	51.55	
39.76	105	5.5	.76	23	63	14	2.00	52.99	
.....	108	1.0	.79	20	56	24	1.72	45.34	Basal.
.....	108	2.5	.77	19	65	16	1.78	46.92	
.....	104	7.7	.75	18	79	13	1.85	48.74	
39.14									
38.89	103	9.6	.77	16	65	19	1.75	45.41	Basal.
38.68	102	9.6	.75	16	70	14	1.76	45.66	
38.88	92	9.5	.74	16	75	9	1.75	45.50	
37.19									
37.16	98	2.6	1.00	15	1	84	1.53	39.92	At 10:19, 115 gm. commercial glucose; second and third periods averaged.
36.63	97	5.1	1.02	15	..	85	1.55	40.19	
37.21	97	6.0							
36.92									
36.88	75	2.5	.92	15	22	63	1.28	33.39	Basal. Asleep most of first hour.
36.60	76	15.6	1.01	13	..	87	1.42	36.90	
.....	91	7.0	.99	28	3	69	1.70	44.90	9.00-10:00, protein meal; 10.2 gm. N. Asleep first period.
.....	90	20.5	1.06	27	..	73	1.75	46.34	
.....	98	6.5(?)	.97	25	8	67	1.91	50.51	
.....	73	6.6	1.02	15	..	85	1.38	36.31	Basal. Asleep one-half first period.
.....	76	14.2	.96	14	11	75	1.51	39.75	
36.61									
36.82	104	5.5	.87	15	37	48	1.46	39.66	Basal. Asleep first period.
37.00	112	13.0	.87	14	40	46	1.65	44.79	
36.76	105	17.3	.82	13	53	34	1.68	45.40	

Subject Date Weight	Period	End of Period	Carbon-dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.	Direct Calorimetry (Rectal Temp.) Cal.	Rectal Temp. C.
Howard F. .... Dec. 30, '13 39.40 kg.	Prelim.	1:30	.....	.....	..	.....	.....	.....	.....	.....	37.29
	1	2:30	19.66	17.18	.83	22.45	0.278	57.68	62.50	55.92	37.10
	2	3:30	20.74	18.62	.81	23.93	0.278	62.21	60.81	61.45	37.17
Karl S. .... Jan. 5, '14 54.64 kg.	Prelim.	11:50	.....	.....	..	.....	.....	.....	.....	.....	40.14
	1	12:50	30.78	29.50	.76	39.97	0.720	96.73	101.70	91.12	39.92
	2	1:50	29.73	28.53	.76	42.23	0.720	93.48	104.45	93.93	39.70
Karl S. .... Jan. 6, '14 54.52 kg.	Prelim.	12:30	.....	.....	..	.....	.....	.....	.....	.....	39.58
	1	1:30	34.01	29.51	.84	26.77	0.879	96.46	87.72	112.04	40.08
	2	2:30	35.13	31.49	.81	34.31	0.879	104.43	104.39	99.22	40.05
	3	3:30	35.32	31.56	.81	33.70	0.879	104.75	107.68	106.06	40.02
Karl S. .... Jan. 16, '14 52.21 kg.	Prelim.	10:50	.....	.....	..	.....	.....	.....	.....	.....	38.29
	1	11:50	26.55	25.94	.74	26.51	0.786	84.44	.....	.....	38.32
	2	1:02	32.49	28.88	.82	38.71	0.943	95.01	.....	.....	38.22
	3	1:50	21.52	19.72	.80	32.34	0.655	64.72	.....	.....	38.14
Karl S. .... Jan. 19, '14 51.19 kg.	Prelim.	10:50	.....	.....	..	.....	.....	.....	.....	.....	36.36
	1	11:50	20.70	16.34	.92	12.72	0.522	55.62	.....	.....	36.54
	2	12:50	22.08	18.41	.87	28.28	0.522	62.03	.....	.....	36.55
	3	1:50	22.53	19.41	.84	32.55	0.522	64.98	.....	.....	36.57
Karl S. .... Jan. 21, '14 51.29 kg.	Prelim.	12:30	.....	.....	..	.....	.....	.....	.....	.....	36.72
	1	1:30	24.09	19.71	.89	32.46	0.858	66.11	.....	.....	36.55
	2	2:30	23.96	19.57	.89	25.79	0.858	65.65	.....	.....	36.39
	3	3:30	26.95	21.45	.91	32.17	0.858	72.55	.....	.....	36.46
Karl S. .... Jan. 22, '14 50.63 kg.	Prelim.	12:40	.....	.....	..	.....	.....	.....	.....	.....	36.75
	1	1:40	18.66	15.37	.88	16.87	0.428	51.92	.....	.....	36.54
	2	2:40	21.01	16.98	.90	20.51	0.428	57.70	.....	.....	36.40
	3	3:40	20.54	17.06	.88	22.17	0.428	57.62	.....	.....	36.48
Karl S. .... Feb. 6, '14 53.30 kg.	Prelim.	11:05	.....	.....	..	.....	.....	.....	.....	.....	37.15
	1	12:05	23.16	20.28	.83	23.98	0.324	68.07	67.32	58.11	36.95
	2	1:05	21.97	18.82	.85	22.85	0.324	63.43	67.46	56.97	36.72
	3	2:05	25.49	24.36	.76	27.16	0.324	80.44	74.45	80.28	36.80
Karl S. .... Feb. 7, '14 54.45 kg.	Prelim.	10:46	.....	.....	..	.....	.....	.....	.....	.....	37.35
	1	11:46	27.92	22.71	.89	32.41	0.581	77.05	77.13	60.51	36.99
	2	12:46	27.83	21.87	.91	29.12	0.581	74.43	79.33	74.46	36.89
	3	1:46	26.23	21.16	.90	32.41	0.581	71.85	79.75	76.71	36.83
Thomas B. .... Oct. 15, '13 73.62 kg.	Prelim.	10:48	.....	.....	..	.....	.....	.....	.....	.....	36.79
	1	11:48	24.87	22.60	.80	23.50	0.505	75.00	48.97	70.72	37.13
	2	12:48	27.05	22.82	.86	24.88	0.505	76.95	56.97	72.61	37.38
	3	1:48	26.46	24.69	.78	26.46	0.505	81.57	63.67	74.67	37.58
	4	2:48	28.39	24.58	.84	28.78	0.505	82.49	67.68	79.68	37.78
Thomas B. .... Oct. 21, '13 72.56 kg.	Prelim.	10:24	.....	.....	..	.....	.....	.....	.....	.....	36.60
	1	11:24	22.98	20.14	.83	24.71	0.407	67.43	.....	52.61	36.71
	2	12:24	24.90	19.11	.95	29.65	0.407	65.88	65.03	63.75	36.71
	3	1:24	26.13	20.21	.94	30.15	0.407	69.58	68.06	62.32	36.64

Surface Temp., C.	Average Pulse	Work Adder., Cm.	Non-Protein, R. Q.	Per Cent. Calories from			Calories Per Hour		Remarks
				Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M.	
36.57									
36.44	109	6.5	.84	13	48	39	1.47	40.49	Basal. Asleep greater part of both periods.
36.60	107	8.5	.81	12	57	31	1.58	43.67	
39.24									
38.97	114	8.4	.75	20	69	11	1.77	54.98	Basal.
38.67	109	6.7	.75	20	69	11	1.71	53.06	
38.60									
39.61	107	8.8	.85	24	39	37	1.80	55.62	9:45-10:12, protein meal; 10.5 gm. N.
39.39	90(?)	14.6	.81	22	50	28	1.92	59.00	
39.27	119	13.0	.82	22	49	29	1.92	59.18	
.....	92	12.2	.72	25	70	5	1.62	49.09	Basal. Water ther. broken. Second period 72 min. long on account movement.
.....	96	21.0+8?	.82	26	44	30	1.53	46.03	
....	96	11.0	.77	26	57	17	1.55	45.15	
.....	76	10.6	.96	25	9	66	1.09	32.74	Basal.
.....	76	14.8+4	.89	22	28	50	1.21	36.51	
.....	78	16.8	.86	21	39	40	1.27	38.25	
.....	73	9.8	.94	34	14	52	1.29	38.89	9:35-11:36, protein meal; 10.0 gm. N.
.....	69	5.7	.94	35	13	52	1.28	38.62	
.....	74	17.0	.97	31	7	62	1.42	42.68	
.....	59	4.0	.91	22	25	53	1.03	30.81	Basal. Asleep first period.
.....	57	11.7	.93	20	20	60	1.14	34.24	
.....	68	9.2	.90	20	29	51	1.14	34.20	
36.20									
36.52	81	15.5	.84	13	49	38	1.28	39.03	Basal. Asleep about 30 min. in first period and 50 min. in second.
35.86	79	9.4	.86	14	42	44	1.19	36.37	
35.97	82	25.2	.76	11	74	15	1.51	46.12	
36.40									
36.58	94	12.4	.92	20	22	58	1.41	43.56	7:30-7:40, 44.3 gm. protein; 9:35-9:37, 15.6 gm. protein; total, 9.6 gm. N. Asleep most of the time.
35.97	90	7.2	.94	21	16	63	1.37	42.07	
36.24	86	11.0	.93	21	19	60	1.32	40.62	
.....	81	8.0	.80	18	56	26	1.02	34.67	Basal.
.....	85	14.0	.88	17	35	48	1.05	35.58	
.....	84	7.6	.77	16	65	19	1.11	37.71	
.....	91	21.0	.85	16	43	41	1.12	38.14	
.....	73(?)	12.0	.84	16	47	37	0.93	31.48	Basal.
.....	78	19.0	.98	16	6	78	0.91	30.76	
.....	84	....	.97	16	9	75	0.96	22.48	

Subject Date Weight	Period	End of Period	Carbon-dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.	Direct Calorimetry (Rectal Temp.) Cal.	Rectal Temp. C.
Richard T. .... Oct. 18, '13 36.49 kg.	Prelim.	9:48	.....	.....	..	.....	.....	.....	.....	.....	38.13
	1	10:48	20.39	18.59	.80	30.29	0.403	61.65	43.77	57.62	38.60
	2	11:48	21.05	18.24	.84	21.24	0.403	61.12	42.57	66.86	39.50
	3	12:48	20.49	18.68	.80	25.61	0.403	61.95 ?	45.94	52.35	39.74
Richard T. .... Oct. 20, '13 35.37 kg.	Prelim.	10:16	.....	.....	..	.....	.....	.....	.....	.....	37.68
	1	11:16	18.98	15.18	.91	31.21	0.499	51.48	42.37	58.44	38.24
	2	12:16	21.25	18.39	.84	31.41	0.499	61.49	47.46	58.51	38.63
	3	1:16	19.90	17.96	.81	29.74	0.499	59.49	48.42	46.90	38.64
Anton K. ...... Oct. 16, '13 50.55 kg.	Prelim.	11:16	.....	.....	..	.....	.....	.....	.....	.....	36.99
	1	12:16	22.48	18.64	.88	30.88	0.479	62.98	61.00	61.00	36.99
	2	1:16	21.65	19.08	.83	33.40	0.479	63.64	66.45	72.34	37.14
	3	2:16	23.57	19.73	.87	30.29	0.479	66.57	64.84	68.64	37.24
Rose G. .... Nov. 22, '13 30.11 kg.	Prelim.	11:04	.....	.....	..	.....	.....	.....	.....	.....	37.04
	1	12:04	17.77	15.73	.82	28.24	.....	52.81	51.24	53.76	37.15
	2	12:34	9.28	7.28	.93	17.44	.....	24.98	28.36	24.99	37.02
Edw. B. .... Oct. 23, '14 55.76 kg.	Prelim.	12:07	.....	.....	..	.....	.....	.....	.....	.....	38.07
	1	1:07	25.02	22.61	.81	30.22	0.187	75.66	62.23	70.20	38.25
	2	2:07	25.51	23.48	.79	28.76	0.187	78.30	64.70	81.43	38.62
	3	3:07	27.24	25.59	.77	29.84	0.187	85.03	70.05	71.67	38.88
Edw. B. .... Oct. 26, '14 56.10 kg.	Prelim.	11:24	.....	.....	..	.....	.....	.....	.....	.....	37.54
	1	12:24	23.13	19.58	.86	31.21	0.264	66.36	61.58	66.23	37.65
	2	1:24	24.87	23.79	.76	29.49	0.264	78.72	60.08	67.98	37.83
	3	2:24	25.18	22.90	.80	30.36	0.264	76.47	65.45	73.84	38.01
	4	3:24	26.12	23.21	.82	31.13	0.264	77.87	70.55	84.46	38.32
Edw. B. .... Oct. 27, '14 56.84 kg.	Prelim.	11:20	.....	.....	..	.....	.....	.....	.....	.....	37.40
	1	12:20	24.80	21.91	.82	30.89	0.552	73.06	60.09	59.69	37.46
	2	1:20	23.76	22.13	.78	29.26	0.552	73.01	61.33	70.63	37.68
	3	2:20	23.24	22.30	.76	28.83	0.552	73.13	63.78	73.06	37.91
Edw. B. .... Nov. 4, '14 58.72 kg.	Prelim.	11:15	.....	.....	..	.....	.....	.....	.....	.....	37.16
	1	12:15	24.00	19.79	.88	31.79	0.337	67.32	64.06	64.69	37.18
	2	1:15	25.03	21.77	.84	31.06	0.337	73.17	65.16	69.21	37.27
	3	2:15	24.89	21.98	.82	31.62	0.337	73.72	70.13	74.19	37.36
Edw. B. .... Nov. 6, '14 59.78 kg.	Prelim.	11:15	.....	.....	..	.....	.....	.....	.....	.....	38.84
	1	12:15	26.21	23.22	.82	27.40	0.336	77.76	62.39	81.16	39.28
	2	1:15	26.65	23.45	.83	28.17	0.336	78.07	64.20	69.44	39.41
	3	2:15	26.61	23.39	.82	30.30	0.336	78.33	68.49	72.75	39.52
Edw. B. .... Nov. 10, '14 56.87 kg.	Prelim.	11:15	.....	.....	..	.....	.....	.....	.....	.....	40.32
	1	12:15	30.59	30.14	.74	35.32	0.525	98.74	88.56	86.50	40.33
	2	1:15	29.52	27.49	.78	36.30	0.525	90.99	87.53	91.26	40.43
	3	2:15	30.25	.....	..	39.54	0.525	.....	94.67	86.34	40.26
John K. .... Dec. 15, '14 63.81 kg.	Prelim	11:56	.....	.....	..	.....	.....	.....	.....	.....	39.00
	1	12:56	30.97	28.17	.80	34.02	1.258	92.29	85.30	94.23	39.26
	2	1:56	30.59	30.06	.74	39.95	1.258	97.14	91.58	87.82	39.22

Surface Temp., C.	Average Pulse	Work Adder., Cm.	Non-Protein, R. Q.	Per Cent. Calories from			Calories Per Hour		Remarks
				Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M.	
.....	81	31.4	.80	17	57	26	1.69	45.50	Basal. Somewhat restless.
.....	98	16.2	.85	17	43	40	1.68	45.11	
.....	..	18.5	.80	17	57	26	1.70	45.72	
.....	82	22.0	.95	26	13	61	1.45	38.79	Basal.
....	102	30.0	.85	22	40	38	1.74	46.34	
.....	95	17.0	.81	22	50	28	1.68	44.83	
.....	76	21.0	.90	20	28	52	1.25	37.42	Basal.
.....	81	19.0	.88	20	46	34	1.26	37.81	
.....	80	13.0	.89	19	32	49	1.32	39.55	
35.75									
36.05	79	16.0	....	..	..	..	1.75	44.82	Basal. Restless. Second period ½ hr. long because patient voided in bed.
36.10	76	9.0	....	..	..	..	1.66	41.93	
.....	118	12.0	.81	7	49	44	1.36	42.10	Basal.
.....	115	17.0	.79	6	67	27	1.40	43.57	
.....	116	24.0	.77	6	73	21	1.58	47.32	
.....	105	11.0	.87	11	39	50	1.18	36.78	10:25 a. m., 79 gm. olive oil = 750 calories.
.....	117	10.0	.76	9	74	17	1.40	43.64	
.....	126	10.0	.80	9	62	29	1.36	42.39	
.....	123	15.0	.82	9	56	35	1.39	43.17	
.....	106	14.0	.83	19	47	34	1.29	40.16	Basal.
.....	109	22.0	.78	19	61	20	1.29	40.12	
.....	107	14.0	.75	19	69	12	1.29	40.18	
.....	102	10.6	.90	13	30	57	1.15	36.19	Basal.
.....	104	14.0	.84	12	48	40	1.25	39.34	
.....	105	25.0	.83	12	51	37	1.26	39.64	
.....	...	31.0	.82	11	54	35	1.30	41.32	Basal. Rising temp.
.....	124	5.0	.83	11	51	38	1.31	41.48	
.....	124	12.0	.82	11	54	35	1.31	41.62	
.....	141	24.0	.73	14	79	7	1.74	54.31	Basal. Very high temp. Mildly delirious.
.....	142	30.5	.78	15	64	21	1.60	50.05	
.....	140	16.0++							
.....	62	16.0	.80	36	43	21	1.45	46.94	Basal.
.....	63	14.0	.70	34	66	0	1.52	49.41	

TABLE 6.—CLINICAL DATA

CHARLES F.

Date, 1913	Food			Food N., Gm.	Urine N., Gm.	Excreta N., Gm.	Nitrogen Bal., Gm.	Body Wt., Kg.	Urine Vol., C.c.
	Total Calories	Carbohydrate, Gm.	Fat, Gm.						
Nov. 6....	1,465	88.0	96.0	8.3	14.68	15.51†	—7.21	58.56	1,270
Nov. 7....	.....	.....	.....	....	15.52	.....	....	.....	1,600
Nov. 8....	1,855	116.0	128.0	9.1	21.10	22.01	—12.91	.....	2,300
Nov. 9....	2,065	130.0	135.0	10.8	20.45	21.58	—10.78	.....	1,870
Nov. 10....	1,088	80.0	69.0	4.4	16.22	16.66	—12.26	57.76	1,205
Nov. 11....	2,027	214.0	87.0	13.2	22.28	23.60	—10.40	58.25	1,740
Nov. 12....	2,610	251.0	144.0	9.8	18.92	19.90	—10.10	.....	2,110
Nov. 13....	2,255	218.0	118.0	10.2	17.37	18.39	—8.19	57.88	1,900
Nov. 14....	1,399	203.0	50.0	3.8	16.08	16.41	—12.61	57.60	1,235
Nov. 15....	1,286	143.0	60.0	4.6	18.54	19.00	—14.40	56.86	1,270
Nov. 16....	1,440	151.0	72.0	5.7	18.89	19.46	—13.76	.....	1,960
Nov. 17....	1,492	128.0	83.0	7.6	17.82	18.58	—10.98	.....	2,110
Nov. 18....	1,749	133.0	107.0	8.1	20.34	21.15	—13.05	56.01	1,470
Nov. 19....	1,019	63.0	68.0	5.2	22.13	22.65	—17.45	.....	1,360
Nov. 20....	1,323	93.0	76.0	8.7	22.41	23.28	—14.58	.....	1,380
Nov. 21....	1,426	74.0	98.0	8.1	22.81	23.62	—15.52	.....	1,380
Nov. 22....	1,970	122.0	128.0	10.9	20.50	21.59	—10.69	.....	1,900
Nov. 23....	1,787	112.0	115.0	10.6	18.16	19.22	—8.62	.....	1,680
Nov. 24....	1,696	117.0	101.0	10.4	18.16	19.20	—8.80	52.02	1,580
Nov. 25....	2,443	159.0	155.0	13.8	18.95	20.38	—6.58	.....	1,910
Nov. 26....	2,595	174.0	160.0	15.4	18.92	20.46	—5.06	51.48	20.50
Nov. 27....	2,345	173.0	142.0	12.3	18.41	19.64	—7.34	.....	1,920
Nov. 28....	2,646	223.0	150.0	13.1	16.65	17.96	—4.86	50.98	2,120
Nov. 29....	* 1,903	129.0	126.0	7.8	13.91	14.69	—6.89	50.29	1,150
Nov. 30....	2,825	236.0	158.0	15.2	15.58	17.10	—1.90	.....	1,700
Dec. 1....	3,491	314.0	195.0	14.9	14.12	15.61	—0.71	50.50	1,760
Dec. 2....	3,126	310.0	160.0	14.3	12.33	13.76	+0.54	.....	1,480+
Dec. 3....	2,595	279.0	118.0	13.7	11.99	13.36	+0.34	50.79	1,600
Dec. 4....	3,408	382.0	150.0	17.4	12.69	14.43	+2.96	.....	1,480
Dec. 5....	2,683	362.0	87.0	15.0	12.05	13.55	+1.45	.....	1,580
Dec. 6....	2,827	390.0	88.0	15.9	12.67	14.26	+1.64	49.83	1.401
Dec. 7....	3,223	446.0	106.0	16.0	12.72	14.32	+1.68	49.83	1,740
Dec. 8....	2,182	346.0	94.0	20.0	16.27	18.27	+1.73	51.02	1,220
Dec. 9....	2,426	308.0	91.0	12.5	12.04	13.29	—0.79	50.41	695
Dec. 10....	2.905	432.0	88.0	12.3	10.01	11.24	+1.06	50.80	1,100
Dec. 11....	3,485	503.0	107.0	16.7	9.47	11.14	+5.56	.....	1,640
Dec. 12....	3,768	556.0	115.0	16.3	9.92	11.55	+4.75	.....	1,500
Dec. 13....	4,025	619.0	129.0	18.2	10.48	12.30	+5.90	53.16	1,380
Dec. 14....	3,660	549.0	105.0	16.8	10.59	12.27	+4.53	.....	1,470

* Estimate heat production 1,725.

TABLE 6.—CLINICAL DATA—(*Continued*)

CHARLES F.—(*Continued*)

Date, 1913	Food			Food N., Gm.	Urine N., Gm.	Excreta N., Gm.	Nitrogen Bal., Gm.	Body Wt., Kg.	Urine Vol., C.c.
	Total Calories	Carbohydrate, Gm.	Fat, Gm.						
Dec. 15....	4.032	585.0	• 124.0	18.8	9.93	11.81	+6.99	52.81	1,330+
Dec. 16....	3.921	573.0	118.0	18.6	11.67	13.53	+5.07	54.05	1,280
Dec. 17....	3,539	510.0	109.0	16.9	11.15	12.84	+4.06	.....	1,470
Dec. 18....	3,869	572.0	113.0	18.2	11.54	13.36	+4.84	.....	1,800
Dec. 19....	4,085	630.0	112.0	17.9	10.39	12.18	+5.72	.....	1,500
Dec. 20....	3,901	599.0	105.0	18.5	11.04	12.89	+5.61	.....	1,760
Dec. 21....	4.017	620.0	105.0	19.3	11.43	13.36	+5.94	.....	1,850
Dec. 22....	3,351	282.0	189.0	17.1	12.33	14.04	+3.06	55.43	1,700
Dec. 23....	3,722	241.0	249.0	16.4	11.46	13.10	+3.30	.....	1,180
Dec. 24....	3,739	228.0	254.0	17.5	13.14	14.89	+2.61	.....	1,440
Dec. 25....	.....	.....	.....	....	9.28	.....	....	.....	1.300
Dec. 26....	2,122	158.0	187.0	12.4	9.40	10.64	+1.76	55.91	1,940
Dec. 27....	3,636	254.0	224.0	20.0	12.16	14.16	+5.84	.....	1,600
Dec. 28....	3,614	247.0	226.0	19.4	12.86	14.80	+4.60	.....	1,640
Dec. 29....	3,818	221.0	259.0	19.0	12.78	14.66	+4.34	.....	1,820
Dec. 30....	4,899	256.0	347.0	24.2	11.49	13.91	+10.29	.....	1,480
Dec. 31....	2,131	202.0	103.0	13.3	11.53	12.86	+0.44	56.43	1,571
1914 Jan. 1....	3,949	347.0	161.0	18.6	11.54	13.40	+5.20	.....	1,000
Jan. 2....	3,587	287.0	202.0	22.0	8.10	10.30	+11.70	.....	860

† Excreta nitrogen estimated as urine nitrogen + 10 per cent. of food nitrogen.

TABLE 6.—CLINICAL DATA—(*Continued*)

MORRIS S.

Date, 1913	Estimated Heat Production per 24 Hrs.	Food Total Calories	Food Carbohydrate, Gm.	Food Fat, Gm.	Food N., Gm.	Urine N., Gm.	Feces N., Gm.	Excreta N., Gm.	Nitrogen Bal., Gm.	Body Weight Kg.	Urine Volume, C.c.	Feces Fat
Oct. 23	.....	2,962	419.0	76.0	20.8	15.13	3.1*	18.2	+2.6	49.69	1,280	
Oct. 24	2,376	1,259	169.0	28.0	11.8	19.56	1.7*	21.3	—9.5	51.50	2,350	
Oct. 25	2,299	2,371	364.0	86.0	21.3	13.59	3.2*	16.8	+4.5	51.22	1,710	
Oct. 26	.....	4,375	471.0	101.0	19.5	20.34	2.9	23.2	—3.7	.....	3,000	
Oct. 27	.....	3,194	321.0	152.0	18.2	21.60	2.7	24.3	—6.1	51.26	2,170	
Oct. 28	2,200	2,332	242.0	116.0	10.0	17.43	1.5	18.9	—8.9	51.18	1,390	
Oct. 29	2,228	2,376	258.0	150.0	16.4	20.38	2.5	22.9	—6.5	50.17	1,465	
Oct. 30	.....	3,031	318.0	141.0	15.5	18.72	2.31	21.03	—5.5	49.85	1,580	9.74
Oct. 31	2,225	2,784	224.0	149.0	18.0	22.28	2.31	24.59	—6.6	50.32	1,330	9.74
Nov. 1	.....	3,089	327.0	147.0	14.8	17.48	2.31	19.79	—5.0	49.32	1,600	9.74
Nov. 2	.....	3,039	324.0	142.0	15.2	16.76	2.31	19.07	—3.9	.....	1,600	9.74
Nov. 3	2,205	3,069	324.0	142.0	15.2	17.39	2.31	19.70	—4.5	48.88	1,370	9,74
Nov. 4	.....	3,069	324.0	142.0	15.2	15.86	2.31	18.17	—3.0	49.63	1,220	9.74
Nov. 5	2,104	3,024	324.0	139.0	15.4	15.57	2.31	17.88	—2.5	48.48	1,160	9.74
Nov. 6	.....	3,039	325.0	147.0	15.4	13.51	2.3	15.8	—0.4	49.03	1,310	
Nov. 7	.....	3,034	327.0	140.0	15.0	12.39	2.3	14.7	+0.3	.....	1,220	
Nov. 8	.....	3,018	319.0	142.0	15.0	11.24	2.3	13.5	+1.5	48.73	1,310	
Nov. 9	.....	3,048	321.0	144.0	15.4	11.71	2.3	14.0	+1.4	.....	1,240	
Nov. 10	.....	2,969	305.0	144.0	14.9	12.05	2.2	14.3	+0.6	.....	2,000	
Nov. 11	.....	3,004	324.0	140.0	14.8	10.23	2.2	12.4	+2.4	48.05	1,220	
Nov. 12	.....	2,998	314.0	142.0	15.2	12.78	2.3	15.1	+0.1	.....	1,380	
Nov. 13	.....	2,998	314.0	142.0	15.2	11.43	2.3	13.7	+1.5	.....	1,480	
Nov. 14	....	3,181	331.0	142.0	15.4	10.54	2.3	12.8	+2.6	.....	1,390	
Nov. 15	.....	2,994	318.0	142.0	15.2	10.42	2.3	12.7	+2.5	.....	2,000	
Nov. 16	.....	3,134	341.0	144.0	15.3	11.44	2.3	13.7	+1.6	.....	1,820	
Nov. 17	1,875	3,076	333.0	142.0	15.2	13.32	2.3	15.6	—0.4	48.80	1,690	
Nov. 18	2,022	1,987	217.0	95.0	8.0	15.19	1.2	16.4	—8.4	49.06	1,440	
Nov. 19	.....	1,855	148.0	61.0	7.7	15.47	1.2	16.7	—9.0	.....	2,280	
Nov. 20	.....	1,727	199.0	79.0	7.0	15.13	1.1	16.2	—9.2	.....	1,300	
Nov. 21	.....	1,805	171.0	95.0	8.4	14.74	1.3	16.0	—7.6	.....	900	
Nov. 22	.....	2,292	153.0	152.0	10.1	14.85	1.5	16.4	—6.3	.....	800	
Nov. 23	.....	2,392	192.0	132.0	10.7	15.69	1.6	17.3	—6.6	.....	840	
Nov. 24	2,282	2,016	178.0	117.0	8.5	13.08	1.3	14.4	—5.9	46.96	890	
Nov. 25	2,301	2,298	187.0	123.0	15.1	13.66	2.3	16.0	—0.9	47.47	925	
Nov. 26	2,217	2,067	172.0	126.0	8.0	10.32	1.2	11.5	—3.5	45.84	780	
Nov. 27	.....	2,747	242.0	148.0	14.8	18.58	2.2	20.8	—6.0	.....	820	
Nov. 28	.....	2,741	256.0	140.0	15.0	12.44	2.3	14.7	+0.3	47.26	980	
Nov. 29	.....	3,033	324.0	142.0	15.0	11.82	2.3	14.1	+0.9	.....	1,370	
Nov. 30	.....	3,158	334.0	147.0	16.0	10.76	2.4	13.2	+2.8	.....	1,060	
Dec. 1	.....	3,091	333.0	142.0	15.7	9.81	2.4	12.2	+3.5	47.03	1,180	
Dec. 2	.....	3,090	340.0	142.0	15.3	9.69	2.3	12.0	+3.3	.....	1,660+	

* Feces analyzed October 30 to November 5. Feces nitrogen averaged 14.8 per cent. of food nitrogen. On all other days the feces nitrogen was calculated as 15 per cent. of food nitrogen.

TABLE 6.—CLINICAL DATA—(*Continued*)

MORRIS S.—(*Continued*)

Date, 1913	Estimated Heat Production per 24 Hrs.	Food: Total Calories	Food: Carbohydrate, Gm.	Food: Fat, Gm.	Food N., Gm.	Urine N., Gm.	Feces N., Gm.*	Excreta N., Gm.*	Nitrogen Balance, Gm.	Body Weight, Kg.	Urine Volume, C.c.	Feces Fat
Dec 3	.....	3,189	356.0	141.0	16.0	8.52	2.4	10.9	+5.1	47.31	930	
Dec. 4	.....	3,118	250.0	180.0	16.0	8.70	2.4	11.1	+4.9	.....	1,500	
Dec. 5	.....	2,977	156.0	209.0	15.0	8.74	2.3	11.0	+4.0	.....	1,520	
Dec. 6	.....	2,998	161.0	209.0	15.0	9.75	2.3	12.1	+2.9	46.55	1,340	
Dec. 7	.....	3,297	202.0	221.0	16.0	9.08	2.4	11.5	+4.5	.....	1,640	
Dec. 8	.....	3,914	206.0	289.0	14.9	8.55	2.2	10.8	+4.1	.....	1,340	
Dec. 9	.....	3,989	219.0	290.0	15.2	7.65	2.3	10.0	+5.2	47.53	1,140	
Dec. 10	.....	3,989	219.0	290.0	15.2	8.85	2.3	11.2	+4.0	.....	1,550	
Dec. 11	.....	3,989	219.0	290.0	15.2	9.31	2.3	11.6	+3.6	48.46	1,350	
Dec. 12	1,357	3,552	222.0	226.0	21.3	9.87	3.2	13.1	+8.2	48.64	1,700	
Dec. 13	1,604	2,925	395.0	104.0	13.1	12.64	2.0	14.6	—1.5	48.10	1,935	
Dec. 14	.....	3,256	475.0	95.0	16.5	9.47	2.5	12.0	+4.5	.....	1,100	
Dec. 15	1,723	3,117	511.0	74.0	13.0	8.68	2.0	10.7	+2.3	47.87	1,229	
Dec. 16	1,703	2,182	275.0	76.0	11.6	10.24	1.7	11.9	—0.3	47.91	802	
Dec. 17	.....	3,985	440.0	198.0	15.5	9.30	2.3	11.6	+3.9	.....	1,240	
Dec. 18	.....	3,499	256.0	224.0	14.4	10.82	2.2	13.0	+1.4	.....	1,670	
Dec. 19	2,058	2,868	248.0	173.0	9.6	11.34	1.4	12.7	—3.1	48.34	1,282	
Dec. 20	2,081	2,748	150.0	190.0	14.1	13.41	2.1	15.5	—1.4	48.55	1,343	
Dec. 21	.....	3,426	204.0	232.0	16.0	17.32	2.4	19.7	—3.7	48.55	1,560	
Dec. 22	2,217	3,084	345.0	140.0	12.2	14.42	1.8	16.2	—4.0	48.50	1,223	
Dec. 23	1,982	2,499	121.0	186.0	10.7	11.94	1.6	13.5	—2.8	48.54	888	
Dec. 24	.....	3,357	206.0	225.0	16.5	13.06	2.5	15.6	+0.9	.....	1,480	
Dec. 25	.....	.....	.....	.....	....	10.90	...	....	.....	.....	1,200	
Dec. 26	.....	3,560	189.0	253.0	17.1	10.48	2.6	13.1	+4.0	49.70	1,680	
Dec. 27	.....	3,180	159.0	227.0	16.4	11.10	2.5	13.6	+2.8	.....	1,930	
Dec. 28	.....	3,128	157.0	224.0	15.5	11.43	2.3	13.7	+1.8	.....	1,740	
Dec. 29	.....	3,109	157.0	222.0	15.5	11.77	2.3	14.1	+1.4	.....	1,880	
Dec. 30	.....	3,277	170.0	235.0	15.5	11.72	2.3	14.0	+1.5	.....	1,710	
Dec. 31	.....	2,990	293.0	143.0	17.9	12.61	2.7	15.3	+2.6	.....	1,600	
1914 Jan. 1	.....	2,991	256.0	166.0	15.4	12.11	2.3	14.4	+1.0	.....	2,120	
Jan. 2	1,567	2,078	141.0	132.0	10.7	10.01	1.6	11.6	—0.9	49.22	1,340	
Jan. 3	.....	3,061	158.0	216.0	15.6	12.27	2.3	14.6	+1.0	.....	2,160	
Jan. 4	.....	3,070	162.0	216.0	15.7	10.40	2.4	12.8	+2.9	.....	1,730	
Jan. 5	.....	.....	.....	.....	....	11.21	...	....	.....	.....	1,580	
Jan. 6	.....	3,044	158.0	215.0	15.5	12.69	2.3	15.0	+0.5	.....	2,330	
Jan. 7	.....	3,045	158.0	215.0	15.5	11.66	2.3	14.0	+1.5	.....	1,800	
Jan. 8	.....	3,068	162.0	215.0	15.6	11.77	2.3	14.1	+1.5	.....	1,460	
Jan. 9	.....	3,063	162.0	215.0	15.6	11.66	2.3	14.0	+1.6	.....	1,600	
Jan. 10	.....	3,475	268.0	208.0	17.3	12.10	2.6	14.7	+2.6	.....	1,460	
Jan. 11	.....	3,739	354.0	191.0	19.8	12.22	3.0	15.2	+4.6	.....	1,560	
Jan. 12	.....	3,551	344.0	177.0	19.5	12.61	2.9	15.5	+4.0	.....	2,350	
Jan. 13	.....	4,198	382.0	222.0	22.1	11.49	3.3	14.8	+7.3	.....	1,520	

* Excreta nitrogen estimated as urine nitrogen + 15 per cent of food nitrogen.

TABLE 6.—Clinical Data—(*Continued*)

Howard F.

Date, 1913	Food			Food N., Gm.	Urine N., Gm.	Excreta N., Gm.	Nitrogen Bal., Gm.*	Body Wt., Kg.	Urine Vol., C.c.
	Total Calories	Carbohydrate, Gm.	Fat, Gm.						
Nov. 6....	1,264	83.0	81.0	6.7	12.83	13.50	—6.80	36.06	970
Nov. 7....	918	62.0	59.0	4.4	12.05	12.49	—8.09	35.74	640
Nov. 8....	1,538	87.0	107.0	7.0	12.75	13.45	—6.45	35.79	840
Nov. 9....	1,454	106.0	88.0	7.7	12.61	13.38	—5.68	.....	760
Nov. 10....	1,401	115.0	78.0	8.1	12.67	13.48	—5.38	.....	680
Nov. 11....	925	93.0	38.0	7.5	13.79	14.54	—7.04	34.60	750
Nov. 12....	950	98.0	40.0	7.3	13.42	14.15	—6.85	35.01	830
Nov. 13....	1,260	134.0	60.0	5.8	12.52	13.10	—7.30	34.22	610
Nov. 14....	580	52.0	30.0	3.4	10.42	10.76	—7.36	.....	500
Nov. 15....	1,152	83.0	69.0	6.6	11.10	11.76	—5.16	33.36	900
Nov. 16....	1.096	150.0	40.0	4.4	9.98	10.42	—6.02	.....	500
Nov. 17....	1,462	123.0	83.0	7.2	9.30	10.02	—2.82	33.12	400
Nov. 18....	1,588	128.0	91.0	8.5	10.20	11.05	—2.55	32.93	590
Nov. 19....	984	63.0	62.0	5.7	10.65	11.22	—5.52	.....	780
Nov. 20....	1,288	74.0	75.0	7.3	10.25	10.98	—3.68	32.57	550
Nov. 21....	1,466	91.0	95.0	8.1	11.32	12.13	—4.03	.....	700
Nov. 22....	1,198	78.0	94.0	8.8	11.12	12.00	—3.20	.....	800
Nov. 23....	1,789	92.0	121.0	11.6	11.15	12.31	—0.71	.....	660
Nov. 24....	1,846	146.0	145.0	10.6	10.82	11.88	—1.28	.....	820
Nov. 25....	2,060	138.0	129.0	11.4	9.81	10.95	+0.45	32.14	940
Nov. 26....	2,686	176.0	168.0	15.7	10.42	11.99	+3.71	.....	780
Nov. 27....	2,240	211.0	118.0	10.9	9.47	10.56	+0.34	.....	570
Nov. 28....	2,742	245.0	145.0	15.0	9.98	11.48	+3.52	32.25	920
Nov. 29....	2,581	211.0	152.0	11.9	8.52	9.71	+2.19	.....	620
Nov. 30....	2,922	273.0	153.0	14.8	9.53	11.01	+3.79	.....	1,220
Dec. 1....	2,581	309.0	112.0	10.6	7.77	8.83	+1.77	.....	870
Dec. 2....	2,298	247.0	110.0	10.0	7.69	8.69	+1.31	33.09	900
Dec. 3....	3,689	423.0	163.0	17.2	9.25	10.97	+6.23	.....	900
Dec. 4....	3,627	441.0	147.0	17.7	9.00	10.77	+6.93	.....	1.180
Dec. 5....	2,671	337.0	81.0	21.0	13.01	15.11	+5.89	34.77	1,500
Dec. 6....	2,476	333.0	83.0	12.9	9.20	10.49	+2.41	33.81	775
Dec. 7....	3,621	496.0	119.0	19.0	10.45	12.35	+6.65	.....	1,500
Dec. 8....	3,391	434.0	112.0	17.8	9.89	11.67	+6.13	.....	1,270+
Dec. 9....	3,042	386.0	108.0	18.0	10.73	12.53	+5.47	35.51	1,300
Dec. 10....	2,986	394.0	101.0	16.8	10.51	12.19	+4.61	.....	1.450
Dec. 11....	3,149	405.0	114.0	17.8	10.79	12.57	+5.23	35.99	1,450
Dec 12....	3,100	417.0	101.0	17.5	10.36	12.11	+5.39	.....	1,610
Dec. 13....	3,544	472.0	122.0	18.5	10.03	11.88	+6.62	36.65	1,280

TABLE 6.—CLINICAL DATA—(*Continued*)

HOWARD F.—(*Continued*)

Date, 1913	Food			Food N., Gm.	Urine N., Gm.	Excreta N., Gm.	Nitrogen Bal., Gm.*	Body Wt., Kg.	Urine Vol., C.c.
	Total Calories	Carbohydrate, Gm.	Fat, Gm.						
Dec. 14....	3,338	402.0	133.0	17.8	11.01	12.79	+5.01	.....	1,880
Dec. 15....	3,280	510.0	130.0	19.2	12.98	14.90	+4.30	37.54	1,890+
Dec. 16....	3,511	444.0	129.0	19.2	13.28	15.20	+4.00	.....	1,580
Dec. 17....	3,170	345.0	139.0	18.0	9.95	11.75	+6.25	39.10	1,720
Dec. 18....	2,008	248.0	78.0	10.5	8.57	9.62	+0.88	37.17	1,600
Dec. 19....	3,550	411.0	144.0	20.3	11.89	13.92	+6.38	.....	2.050
Dec. 20....	2,671	110.0	197.0	15.0	8.10	9.60	+5.40	.....	1,540
Dec. 21....	2,383	104.0	175.0	12.6	10.65	11.91	+0.69	.....	1,250
Dec. 22....	2,936	159.0	198.0	17.3	13.23	14.96	+2.34	37.21	1,150
Dec. 23....	3,520	239.0	235.0	13.9	9.19	10.58	+3.32	.....	1,200
Dec 24....	3,605	219.0	243.0	17.4	10.70	12.44	+4.96	.....	1,700
Dec. 25....	.....	.....	.....	....	10.42	.....	......	.....	1,370
Dec. 26....	3,152	219.0	199.0	15.6	9.77	11.33	+4.27	39.46	2,100
Dec. 27....	3,303	257.0	196.0	16.8	10.03	11.71	+5.09	.....	1.600
Dec. 28....	2,946	200.0	186.0	15.4	7.51	9.05	+6.35	.....	1.080
Dec. 29....	4,199	265.0	278.0	20.5	10.87	12.92	+7.58	.....	1,640
Dec. 30....	2,825	165.0	145.0	11.4	7.81	8.95	+2.45	39.39	987
Dec. 31....	3,569	317.0	192.0	18.5	11.77	13.62	+4.88	.....	1,500
1914 Jan. 1....	2,912	236.0	169.0	14.5	9.02	10.47	+4.03	.....	1,600
Jan. 2....	2,891	224.0	156.0	16.0	8.74	10.34	+5.66	.....	1,540

* Excreta nitrogen estimated as urine nitrogen + 10 per cent of food nitrogen.

TABLE 6.—CLINICAL DATA—(*Continued*)

KARL S.

Date, 1914	Estimated Heat Production per 24 Hrs.	Food: Total Calories	Food: Carbohydrate, Gm.	Food: Fat, Gm	Food N., Gm.	Urine N., Gm.	Feces N., Gm.	Excreta N., Gm.*	Nitrogen Balance, Gm.	Body Weight, Kg.	Urine Volume, C.c.
Jan. 3	.....	2,038	104.0	145.0	10.8	20.52	...	21.60	—10.80	.....	880
Jan. 4	.....	1,301	113.0	71.0	6.9	21.72	...	22.41	—15.51	.....	1,240
Jan. 5	2,579	1,119	95.0	64.0	5.4	.....	...	.....	......	54.67	725
Jan. 6	2,707	1,332	167.0	82.0	13.6	22.36	...	23.72	—10.12	54.81	1,010
Jan. 7	.....	1,942	93.2	136.0	11.3	.....	...	.....	......	.....	810
Jan. 8	.....	2,331	136.0	156.0	12.5	16.03	...	17.28	—4.78	.....	860
Jan. 9	.....	1,892	114.0	126.0	9.8	23.84	...	24.82	—15.02	52.99	1,700
Jan. 10	.....	2,910	223.0	174.0	14.6						
Jan. 11	.....	3,018	318.0	139.0	16.4						
Jan. 12	.....	3,017	322.0	138.0	16.2	18.15	1.6	19.8	—3.6	.....	2,310
Jan. 13	.....	2,966	326.0	128.0	17.2	13.94	1.7	15.6	+1.6	.....	1,820
Jan. 14	.....	2,802	313.0	118.0	16.4	17.06	1.6	18.7	—2.3	.....	1,830
Jan. 15	.....	3,129	323.0	149.0	16.2	18.65	1.6	20.3	—4.1	52.74	1,920
Jan. 16	2,206	2,448	226.0	132.0	11.5	19.11	1.2	20.3	—8.8	52.24	1,960
Jan. 17	.....	3,398	340.0	166.0	17.9	19.16	1.8	21.0	—3.1	.....	1,940
Jan. 18	.....	3,138	329.0	145.0	17.1	17.26	1.7	19.0	—1.9	.....	1,920
Jan. 19	1,651	2,795	268.0	145.0	13.6	14.72	1.4	16.1	—2.5	51.21	1,260
Jan. 20	.....	2,965	318.0	138.0	15.7	14.51	1.6	16.1	—0.4	.....	1,550
Jan. 21	1,798	2,912	315.0	129.0	16.3	17.57	1.6	19.2	—2.9	51.52	1,870
Jan. 22	1,512	2,605	258.0	133.0	12.8	13.25	1.3	14.6	—1.8	51.18	1,194
Jan. 23	.....	3,083	324.0	140.0	15.9	11.99	1.6	13.6	+2.3	.....	1,360
Jan. 24	.....	2,982	315.0	138.0	15.8	13.06	1.6	14.7	+1.1	.....	1,960
Jan. 25	.....	2,987	315.0	139.0	15.8	13.17	1.6	14.8	+1.0	.....	1,400
Jan. 26	.....	3,541	408.0	155.0	16.7	12.64	1.7	14.3	+2.4	54.64	1,620
Jan. 27	.....	3,999	439.0	191.0	16.3	13.06	1.6	14.7	+1.6	.....	1,460
Jan. 28	.....	4,025	439.0	194.0	16.3	11.88	1.6	13.5	+2.8	.....	1,280
Jan. 29	.....	3,975	433.0	190.0	16.1	11.32	1.6	12.9	+3.2	52.54	1,450
Jan. 30	.....	3,991	439.0	191.0	16.2	10.65	1.6	12.3	+3.9	.....	1,500
Jan. 31	.....	3,922	418.0	193.0	16.2	10.93	1.6	12.5	+3.7	.....	1,400
Feb. 1	.....	3,940	418.0	194.0	16.3	10.63	1.6	12.2	+4.1	.....	1,500
Feb. 2	.....	3,808	419.0	180.0	16.0	11.21	1.6	12.8	+3.2	.....	1,910
Feb. 3	.....	3,808	419.0	180.0	16.0	11.15	1.6	12.8	+3.2	.....	1,980
Feb. 4	.....	3,971	442.0	188.0	16.0	10.87	1.6	12.5	+3.5	.....	1,870
Feb. 5	.....	3,974	438.0	191.0	16.0	9.29	1.6	10.9	+5.1	.....	1,640
Feb. 6	1,916	3,232	330.0	165.0	13.3	10.24	1.3	11.5	+1.8	53.33	1,360
Feb. 7	1,965	3,526	387.0	148.0	22.1	.....	2.2	17.3	+4.8	54.48	2,300
Feb. 8	.....	4,018	474.0	178.0	16.3	11.67	1.6	13.3	+3.0	.....	1,440

* Excreta nitrogen estimated as urine nitrogen + 10 per cent. of food nitrogen.

TABLE 6.—CLINICAL DATA—(*Continued*)
THOMAS B.

Date 1913	Temperature Max.	Temperature Min.	Food: Total Calories	Food: Carbo-hy-drate, Gm.	Food: Fat, Gm.	Food N., Gm.	Urine N., Gm.	Feces N., Gm.	Excreta N., Gm.	Nitrogen Balance, Gm.	Body Weight, Kg.	Urine Volume, C.c.	Feces Fat
Oct. 7	103.0	101.4	3,052	168.0	212.0	15.0	24.55	2.09	26.64	—11.64	76.06	1,240	9.19
Oct. 8	103.6	101.2	3,010	163.0	210.0	15.0	25.50	2.09	27.59	—12.59	75.61	1,270	9.19
Oct. 9	104.0	101.6	3,010	163.0	210.0	15.0	21.29	2.09	23.38	—8.38	75.73	1,120	9.19
Oct. 10	103.6	101.6	3.030	168.0	212.0	15.0	23.67	2.09	25.76	—10.76	76.02	1,740	9.19
Oct. 11	103.0	101.0	3.014	479.0	71.0	14.9	20.12	1.89	22.01	—7.11	74.85	1,500	5.80
Oct. 12	102.8	101.6	3,018	480.0	71.0	15.0	17.77	1.89	19.66	—4.66	.....	1,960	5.80
Oct. 13	102.4	100.6	3,014	479.0	71.0	14.9	18.77	1.89	20.66	—5.76	74.24	1,980	5.80
Oct. 14	103.0	100.0	3.045	173.0	212.0	14.2	18.21	1.28	19.49	—5.29	74.38	1,220	5.02
Oct. 15	102.2	98.6	2,570	180.0	187.0	11.7	18.61	1.28	19.89	—8.19	.....	1,040	5.02
Oct. 16	101.0	99.4	3,058	168.0	212.0	15.4	21.04	1,28	22.32	—6.92	.....	1,010	5.02
Oct. 17	101.6	99.4	3,211	484.0	78.0	15.6	17.79	....	19.35*	—3.75	73.10	1,120	
Oct. 18	100.6	99.0	2,998	476.0	71.0	15.0	15.69	....	17.19	—2.19	.....	1,100	
Oct. 19	99.6	98.6	3,019	481.0	71.0	15.0	15.30	....	16.80	—1.80	.....	1,220	
Oct. 20	99.6	98.6	3,002	468.0	75.0	15.0	15.24	....	16.74	—1.74	72.82	1,880	
Oct. 21	98.6	99.4	2,675	412.0	68.0	13.0	15.75†	....	.....	....	.....	1,610+	(?)
Oct. 22	99.6	98.8	2,943	462.0	71.0	15.0	16.32	....	17.82	—2.82	.....	1,430	
Oct. 23	99.6	98.6	3,062	449.0	76.0	21.2	16.76	....	18.88	+2.32	.....	1,230	
Oct. 24	99.6	98.6	3,396	541.0	60.0	20.0	13.34	....	15.34	+4.66	72.86	1,640	
Oct. 25	99.6	98.6	3,211	493.0	71.0	20.0	16.59	....	18.59	+1.41	.....	1,120	
Oct. 26	99.0	98.2	3,066	164.0	215.0	15.5	18.90	....	20.45	—4.95	.....	1,320	
Oct. 27	99.6	98.4	3,159	164.0	219.0	17.5	17.65	....	19.40	—1.90	.....	2,280	
Oct. 28	99.0	98.2	3,277	182.0	220.0	18.5	14.18	....	16.03	+2.47	73.69	1,220	

† This is the total for 19¾ hours.
* Excreta nitrogen estimated as urine nitrogen + 10 per cent. of food nitrogen.

TABLE 6.—CLINICAL DATA—(*Continued*)
RICHARD T.

Date 1913	Temperature Max.	Temperature Min.	Food: Total Calories	Food: Carbo-hy-drate, Gm.	Food: Fat, Gm.	Food N., Gm.	Urine N., Gm.	Feces N., Gm.	Excreta N., Gm.	Nitrogen Balance, Gm.	Body Weight, Kg.	Urine Volume, C.c.	Feces Fat
Oct. 17	103.6	101.4	1.656	248.0	38.0	11.3	13.95	0.84	14.79	—3.49	36.09	2,290	1.63
Oct. 18	104.2	100.8	1,143	115.0	49.0	8.4	12.48	0.84	13.32	—4.92	.....	1,145	1.63
Oct. 19	103.2	100.8	2,131	327.0	49.0	13.0	14.40	0.84	15.24	—2.24	.....	1,720	1.63
Oct. 20	104.0	100.0	2,020	280.0	55.0	14.0	14.53	0.84	15.37	—1.37	.....	1,005	1.63
Oct. 21	102.8	100.0	2,359	360.0	51.0	16.0	15.13	0.84	15.97	+0.03	.....	1,320	1.63
Oct. 22	102.4	99.4	2,092	315.0	46.0	14.7	14.74	0.84	15.58	—0.88	35.57	1,200	1.63
Oct. 23	103.0	99.0	2,576	369.0	67.0	17.4	16.30	0.84	17.14	+0.26	35.70	1,570	1.63
Oct. 24	102.0	99.4	2,153	333.0	35.0	18.0	15.69	0.84	16.53	+1.47	.....	1,340	1.63
Oct. 25	101.0	98.4	2,519	228.0	125.0	16.0	16.32	0.84	17.16	—1.16	.....	1,260	1.63
Oct. 26	100.6	99.0	2,093	115.0	133.0	15.0	16.53	....	* 18.03	—3.03	.....	1,100	
Oct. 27	100.2	98.6	2,163	121.0	136.0	15.7	16.34	....	17.91	—2.21	35.30	1,200	
Oct. 28	99.6	98.6	2,009	124.0	117.0	16.0	16.47	....	18.07	—2.07	35.60	1,460	
Oct. 29	100.0	98.6	3,276	348.0	157.0	15.2	14.01	....	15.53	—0.33	.....	1,370	
Oct. 30	100.0	99.0	2,969	302.0	144.0	15.1	11.77	....	13.28	+1.82	35.38	1,195	
Oct. 31	101.6	99.2	2,954	310.0	142.0	15.5	12.05	....	13.60	+1.90	.....	1,420	
Nov. 1	102.0	100.4	3,069	334.0	142.0	14.5	11.32	....	12.77	+1.73	36.08	1,320	
Nov. 2	102.4	99.6	2,995	325.0	138.0	14.5	11.74	....	13.19	+1.31	.....	1,900	
Nov. 3	101.0	99.6	2,984	316.0	140.0	15.1	11.99	....	13.50	+1.60	36.27	1,270	
Nov. 4	100.2	99.4	3,037	320.0	144.0	15.2	12.22	....	13.74	+1.46	36.42	1,560	

* Excreta nitrogen estimated as urine nitrogen + 10 per cent. of food nitrogen.

TABLE 6.—CLINICAL DATA—(*Continued*)
EDWARD B.

Date, 1914	Estimated Heat Production per 24 Hrs.	Food			Food N., Gm.	Urine N., Gm.	Excreta N., Gm.*	Nitrogen Balance Gm.	Body Weight, Kg.	Urine Volume, C.c.
		Total Calories	Carbohydrate, Gm.	Fat, Gm.						
Oct. 14	.....	3,901	214.9	284.8	14.5	14.51	15.96	—1.46	56.29	1,180
Oct. 15	.....	4,171	212.9	309.3	16.4	11.39	13.03	+3.4	.....	1.415
Oct. 16	.....	4,003	662.0	97.2	15.0	11.49	12.99	+2.0	56.36	1,665(?)
Oct. 17	.....	1,561	236.3	43.8	7.28	8.65	9.37	—2.09	56.94	1,140
Oct. 18	.....	2,976	94.5	236.9	15.0	11.08	12.58	—2.42	56.01	1,690
Oct. 19	.....	4,217	111.0	362.1	13.9	16.17	17.56	—3.66	56.98	2,230
Oct. 20	.....	4,097	114.9	348.9	14.80	10.96	12.44	+2.36	56.57	1.520
Oct. 21	.....	3,586	518.9	114.7	15.20	9.17	10.69	+4.51	57.21	1,250
Oct. 22	.....	3,076	579.6	54.2	7.68	7.85	8.61	—0.93	56.60	1,170
Oct. 23	2,160	3,462	152.8	269.1	12.90	8.21	9.50	+3.40	55.76	835
Oct. 24	.....	4,072	220.6	299.4	15.0	11.94	13.44	+1.56	56.84	1,465
Oct. 25	.....	4,114	220.9	303.1	15.1	11.20	12.70	+2.40	56.78	1,515
Oct. 26	1,976	2,704	151.4	124.1	6.9	6.75	7.44	—0.54	.....	668
Oct. 27	1,982	3,844	109.1	334.5	11.1	8.61	9.72	+1.38	.....	1,125
Oct. 28	.....	4,056	223.4	295.7	15.2	8.19	9.71	+5.49	57.51	2,155
Oct. 29	.....	4,185	314.8	265.7	16.5	8.70	10.35	+6.15	57.46	1,960
Oct. 30	.....	3,643	364.7	179.0	18.8	10.30	12.18	+6.62	57.83	2.310
Oct 31	.....	3,893	402.5	191.4	18.0	9.72	11.52	+6.48	.....	1.655
Nov. 1	.....	4,394	455.7	218.4	19.3	11.05	12.98	+6.32	58.53	2,450
Nov. 2	.....	4,491	451.6	225.8	21.0	11.80	13.9	+7.1	58.76	1,770
Nov. 3	.....	4,836	491.9	244.6	21.2	12.20	14.32	+6.88	59.52	2,405
Nov. 4	1,936	2,209	209.4	119.7	9.2	9.20	10.12	—0.92	.....	979
Nov. 5	.....	3,960	390.5	195.9	17.0	10.59	12.29	+5.71	.....	1,665
Nov. 6	2,117	1,907	219.5	85.9	8.0	10.96	11.76	—3.76	.....	1,523
Nov. 7	.....	1,006	101.2	49.8	5.05	12.13	12.63	—7.58	59.23	1.075
Nov. 8	.....	398	64.0	11.8	1.08	10.34	10.44	—9.36	.....	665
Nov. 9	.....	617	94.8	20.0	1.68	11.26	11.42	—9.74	57.06	645
Nov. 10	2,632	1,103	104.8	51.2	6.0	14.72	15.32	—9.32	.....	833
Nov. 11	.....	1,646	96.0	84.2	9.7	16.73	17.70	—8.0	57.11	1,230
Nov. 12	.....	2,196	165.9	119.3	10.7	14.79	15.8	—5.1	.....	1,250

* Excreta nitrogen estimated as urine nitrogen + 10 per cent. of food nitrogen.

TABLE 6.—CLINICAL DATA—(*Continued*)
JOHN K.

Date, 1913	Total Calories	Carbohydrate, Gm.	Fat, Gm.	Food N., Gm.	Urine N., Gm.	Excreta N., Gm.	Nitrogen Bal., Gm.	Body Wt., Kg.	Urine Vol., C.c.
Dec. 15....	* 2,194	139.1	148.9	9.3	24.58	25.51	—16.21	63.81	1,152
Dec. 16....	3,309	145.1	246.8	16.3	21.45	23.08	—6.78	63.55	1,180
Dec. 17....	3,521	181.9	258.1	14.6	22.37	23.83	—9.23	63.27	3,110
Dec. 18....	3,205	181.9	223.6	14.8	19.30	20.78	—5.98	63.35	3,040
Dec. 19....	3,788	251.6	249.6	17.0	19.40	21.10	—4.10	63.05	3,230
Dec. 20....	3,916	259.7	257.1	18.0	18.26	20.06	—2.06	62.37	3,460
Dec. 21....	4,134	342.5	238.4	20.0	19.33	21.33	—1.33	63.04	4,285
Dec. 22....	4,558	378.4	267.2	20.4	18.00	20.04	+0.36	62.64	4,255
Dec. 23....	4,838	393.9	285.8	22.0	17.93	22.13	—0.13	63.26	3,210
Dec. 24....	4,450	373.1	259.1	19.9	18.78	20.77	—0.87	63.32	3,350

* Estimated heat production, 2,568 calories.

TABLE 7.—SUMMARY OF CLINICAL CALORIMETRY IN TYPHOID FEVER

Subject and Date	Character of Experiment	Period of Disease	Average Rectal Temp. C.	Average Pulse Rate	Average Respiratory Quotient	Indirect Calorimetry Average per Hour		Per Cent. Divergence of Direct Cal. from Indirect Calories		Per Cent. Rise Above Normal Aver. Basal of 34.7 Cal. per Sq. M.	Per Cent. Rise Above Patient's Own Basal Metabolism	Day of Basal Determination Used for Comparison
						Cal. per Kg.	Cal. per Sq. M.	According to Rectal Temp.	According to Surface Temp.			
Morris S. 25	9.0 gm. N..........	Continued temperature	40.0	99	.77	1.70	51.42	— 5	......	+48		
Oct. 24, 1913	Basal.............	Continued temperature	39.5	101	.84	1.70	51.27	— 2	......	....	— 0.3	Oct. 24.
28	115.0 gm. glucose..	Continued temperature	39.2	111	.98	1.64	49.35	+ 1	......	....	+ 0.6	Oct. 29.
29	Basal.............	Continued temperature	39.6	106	.79	1.62	49.04	— 1	......	+41		
31	10.3 gm. N.........	Early steep curve.......	39.1	100	.84	1.68	50.24	—11	......	....	+ 2.4	Oct. 29.
Nov. 3	Restless...........	Early steep curve.......	38.9	108	.80	1.66	49.46	— 9	......	+43		
5	Basal.............	Early steep curve.......	38.1	106	.81	1.60	47.31	— 4	......	+36		
17	Basal.............	First Relapse Ascending temperature	38.7	108	.81	1.44	42.52	— 1	+ 1	+23		
18	Basal.............	Ascending temperature	39.9	118	.83	1.53	45.38	+ 1	— 1	+31		
24	Basal.............	Continued temperature	39.4	124	.76	1.79	52.69	—17	......	+52		
25	8.7 gm. N..........	Continued temperature	39.2	118	.81	1.84	54.17	— 8	......	....	+ 3.9	Av. Nov. 24 and 26.
26	Basal.............	Early steep curve.......	39.1	118	.76	1.78	51.60	—17	......	+49		
Dec. 12	10.6 gm. N.........	7th day, normal temp.	37.0	94	.84	1.45	42.89	— 9	— 8	....	+18.1	Dec. 13.
13	Basal.............	8th day, normal temp.	37.0	83	.82	1.23	36.83	+ 0	+ 4	+ 5		
15	115 gm. glucose....	10th day, normal temp.	37.2	95	1.01	1.36	40.07	— 8	—11	....	+ 3.7	Dec. 16.
16	Basal.............	11th day, normal temp.	37.3	88	.88	1.31	38.67	— 2	+ 0	+11		
19	115 gm. glucose....	Second Relapse Ascending temperature	39.4	116	.93	1.60	47.46	+ 2	— 4	....	+ 1.3	Dec. 20.
20	Basal.............	Early steep curve.......	39.6	113	.78	1.61	46.83	— 1	— 2	+35		
22	115 gm. glucose....	Early steep curve.......	39.2	116	.94	1.55	46.04	+11	+10	....	+ 0.7	Av. Dec. 20 and 26.
23	Basal.............	Early steep curve.......	38.3	101	.79	1.50	44.57	+ 5	+ 2	+28		
Jan. 2, 1914	Basal.............	8th day, normal temp.	37.0	75	.81	1.17	34.93	+ 3	+ 5	+ 1		
27	Basal.............	33d day, normal temp.	36.9	66	.82	1.10	34.30	+ 7	+ 4	—1		
Dec. 17, 1914	Basal.............	One year later.........	36.8	63	.81	1.10	35.16	+ 0	......	+ 1		
18	9.6 gm. N..........	One year later.........	36.9	68	.88	1.16	37.44	+ 4	......	....	+ 6.5	Dec. 17, 1914.

TABLE 7.—SUMMARY OF CLINICAL CALORIMETRY IN TYPHOID FEVER—(*Continued*)

Subject and Date	Character of Experiment	Period of Disease	Average Rectal Temp. C.	Average Pulse Rate	Average Respiratory Quotient	Indirect Calorimetry Average per Hour		Per Cent. Divergence of Direct Cal. from Indirect Calories		Per Cent. Rise Above Normal Aver. Basal of 34.7 Cal. per Sq. M.	Per Cent. Rise Above Patient's Own Basal Metabolism	Day of Basal Determination Used for Comparison
						Cal. per Kg.	Cal. per Sq. M.	According to Rectal Temp.	According to Surface Temp.			
Charles F. Nov. 10, 1913	Basal.............	Ascending temperature	39.1	78	.79	1.44	45.26	− 7	− 6	+30		
11	6.6 gm. N..........	Ascending temperature	39.2	82	.84	1.50	47.28	+ 1	− 2	....	+ 4.5	Nov. 10, 1913.
14	115 gm. glucose....	Continued temperature	39.5	97	.90	1.54	48.12	− 8	− 6	....	+ 1.3	Nov. 15.
15	Basal.............	Continued temperature	39.9	89	.78	1.52	47.49	−10	− 9	+37		
29	Basal.............	Early steep curve.......	36.9	83	.82	1.29	38.54	+ 2	......	+11		
Dec. 8	10.5 gm. N.........	7th day, normal temp.	36.8	77	.92	1.38	41.53	− 3	......	....	+15.5	Dec. 9.
9	Basal.............	8th day, normal temp.	36.8	78	.92	1.20	35.06	+ 3	......	+ 4		
10	115 gm. glucose....	9th day, normal temp.	36.7	80	1.00	1.33	40.18	−10	......	....	+11.7	Dec. 9.
26	Basal............	25th day, normal temp.	36.9	76	.85	1.17	36.36	+ 8	+ 1	+ 5		
31	Basal.............	30th day, normal temp.	37.0	80	.79	1.21	37.52	− 5	− 8	+ 8		
Howard F. Nov. 7, 1914	Basal..............	Ascending temperature	39.7	103	.78	1.85	49.93	−10	− 3	+44		
12	6.5 gm. N..........	Continued temperature	39.9	105	.81	1.98	51.15	− 2	+ 1	....	+ 8.9	Nov. 13.
13	Basal.............	Continued temperature	39.8	107	.78	1.78	47.00	− 2	− 2	+35		
20	Basal.............	Continued temperature	39.2	99	.76	1.76	45.52	− 2	− 0	+31		
Dec. 1	115 gm. glucose....	5th day, normal temp.	37.0	97	.97	1.54	40.10	− 8	......	....	+14.1	Dec. 2.
2	Basal.............	6th day, normal temp.	36.9	76	.94	1.35	35.15	+ 6	......	+ 1		
5	10.2 gm. N.........	9th day, normal temp.	37.1	91	.85	1.79	47.25	− 2	......	....	+24.3	Dec. 6.
6	Basal.............	10th day, normal temp.	37.0	75	.96	1.45	38.03	+ 0	......	+10		
18	Basal.............	22d day,* normal temp.	37.2	107	.84	1.60	43.28	+ 1	+ 1	+25		
30	Basal.............	34th day,* normal temp.	37.2	108	.82	1.52	42.08	− 2	+ 2	+21		

Karl S. Jan. 5, 1914	Basal..............	Continued temperature	39.9	112	.76	1.74	54.01	— 8	— 6	+56		
6	10.5 gm. N.........	Continued temperature	39.9	108	.82	1.88	57.98	+ 3	+ 6	....	+ 7.3	Jan. 5.
16	Basal.............	Late steep curve......	38.2	95	.79	1.57	46.76	......	......	+35		
19	Basal.............	1st day, normal temp.	36.5	77	.88	1.19	35.83	......	......	+ 3		
21	10.0 gm. N.........	3d day, normal temp.	36.5	72	.90	1.33	40.06	......	......	....	+21.1	Jan. 22.
22	Basal.............	4th day, normal temp.	36.5	61	.89	1.10	33.08	......	......	— 5		
Feb. 6	Basal.............	18th day, normal temp.	36.9	81	.81	1.38	40.51	— 8	— 6	+17		
7	9.6 gm. N..........	19th day, normal temp.	37.0	90	.90	1.37	42.08	— 5	+ 2	....	+ 3.9	Feb. 6.
Thomas B. Oct. 15, 1913	Basal..............	Late steep curve........	37.1	85	.82	1.07	36.54	— 6	......	+ 5		
21	Basal.............	1st day, normal temp.	36.9	78	.92	0.98	31.57	+ 2	......	— 9		
Richard T. Oct. 18, 1913	Basal..............	Early steep curve.......	39.0	90	.81	1.69	45.44	— 4	......	+31		
20	Basal.............	Early steep curve.......	38.3	98	.85	1.62	43.32	— 5	......	+25		
Anton K. Oct. 16, 1913	Basal..............	Late steep curve........	37.1	79	.86	1.27	38.26	+ 5	......	+10		
Rose G. Nov. 22, 1913	Basal..............	25th day, normal temp.	37.1	78	.87	1.71	43.18	+ 1	......	+24		
Edward B. Oct. 23, 1914	Basal.............	First relapse: early steep curve	38.5	116	.79	1.43	44.33	— 7	......	+28		
26	79 gm. olive oil...	First relapse: late steep curve	37.9	118	.81	1.33	41.50	— 2	......	....	+ 3.4	Oct. 27.
27	Basal.............	First relapse: late steep curve	37.6	107	.79	1.29	40.15	— 7	......	+16		
Nov. 4	Basal.............	4th day, normal temp.	37.2	104	.85	1.22	38.89	— 8	......	+12		
6	Basal.............	Second relapse: ascending temp.	39.3	124	.82	1.81	41.47	— 5	......	+20		
10	Basal (irrational)	Second relapse: continued temp.	40.3	141	.76	1.67	52.18	— 6	......	+50		
John K. Dec. 15, 1914	Basal.............	Continued temperature	39.2	63	.77	1.49	48.18	— 4	......	+39		

* Excluded from averages on account of rapid, irregular and weak heart action.

amounts of heat. Therefore the law of the conservation of energy applies to fever patients.

The rectal temperature does not always give an accurate indication of the average change in body temperature, and better results are often obtained by well covered surface thermometers.

The basal heat production rises and falls in a curve roughly parallel with the temperature. At the height of the fever it averages about 40 per cent. above the normal but in some cases rises to more than 50 per cent. above the normal.

The specific dynamic action of protein and carbohydrate is much smaller in the febrile period of typhoid than in health and in some cases seems to be absent. In convalescence it may be greater than normal.

In a majority of cases a rise in temperature is accompanied by an increasing heat production and an increasing heat elimination.

Typhoid patients can store body fat on an abundant diet while losing body weight and body protein. Loss in weight and loss of protein are usually though not necessarily parallel.

There is a toxic destruction of protein in typhoid fever. This is shown by the fact that patients have a distinctly negative nitrogen balance on a diet which contains more than enough calories to cover the heat production.

The writers wish to express their thanks to their associates, without whose assistance this work would have been impossible. The analyses of food and urine were made by Mr. Frank C. Gephart, with the assistance of Messrs. R. H. Harries, L. C. Mazzola and R. H. Stone; all the electrical measurements in the calorimeter experiments were made by Mr. G. F. Soderstrom. We are indebted to Mr. R. H. Harries and Dr. A. L. Meyer for making the residual analyses of air in the calorimeter experiments and for making most of the calculations, and to Miss G. W. Sims for the painstaking work in checking all these calculations. We are indebted to Miss Estelle Magill and to her assistants, especially Miss A. Honold and Miss M. M. Fauquier, for their skillful administration of the diets and for the collection of the specimens. We wish also to thank Miss M. Sawyer for her aid in the preparation of the charts.

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CLINICAL CALORIMETRY

EIGHTH PAPER

ON THE DIABETIC RESPIRATORY QUOTIENT *

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The respiratory quotient, or the ratio of the volume of carbon dioxid expired to the volume of oxygen inspired, in the case of protein oxidation is stated by Loewy[1] to be 0.801. This relation depends on the net result of the oxidation of the many amino-acids of which protein is composed. It is apparent that when some of these amino-acids are converted into glucose which is eliminated in the urine, the respiratory quotient for protein will not hold true. It has been shown[2] that the carbon of glycocoll and alanin is completely converted into glucose in the diabetic organism, and that three of the carbon atoms which are contained in aspartic and glutamic acids are similarly convertible into glucose. Dakin[3] states that prolin and arginin yield glucose comparable in quantity to that yielded by glutamic acid. According to this author cystin and serin also yield glucose.

The reactions involving the conversion of amino-acids into sugar and urea may thus be written:[4]

Glycocoll .... $6CH_2NH_2.COOH + 3CO_2 + 3H_2O = 2C_6H_{12}O_6 + 3CH_4N_2O + 3O_2$

Alanin .... $2CH_3.CHNH_2.COOH + CO_2 + H_2O = C_6H_{12}O_6 + CH_4N_2O$

Aspartic Acid..... $2COOH.CH_2.CHNH_2.COOH + H_2O = C_6H_{12}O_6 + CH_4N_2O + CO_2$

Glutamic Acid..... $2COOH.CH_2.CH_2.CHNH_2COOH + 3O_2 = C_6H_{12}O_6 + CH_4N_2O + 3CO_2 + H_2O$

Prolin .... $2\underbrace{CH_2.CH_2.CH_2.CH}_{NH}.COOH + 5O_2 = C_6H_{12}O_6 + CH_4N_2O + 3CO_2 + H_2O$

Arginin .... $2NH_2.\underset{NH}{\overset{\cdot\cdot}{C}}.NH.CH_2.CH_2.CH_2.CHNH_2COOH + 5O_2 = C_6H_{12}O_6 + 4CH_4N_2O + 2CO_2$

Osborne and Jones[5] have reported an analysis of 100 grams of ox meat containing 16.18 per cent. of total nitrogen. This analysis will

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1. Loewy: Handb. d. Biochem., 1911, iv, No. 1, 279.
2. Ringer and Lusk: Ztschr. f. physiol. Chem., 1910, lxvi, 106.
3. Dakin: Jour. Biol. Chem., 1913, xiv, 321.
4. For more complete theoretical details consult: Lusk, Jour. Am. Chem. Soc., 1910, xxxii, 671; and Dakin and Dudley, Proc. Seventeenth Internat. Cong. Med., 1914, Sec. ii, Part II, 127.
5. Osborne and Jones: Am. Jour. Physiol., 1909, xxiv, 438.

be found below together with the respiratory quotients, both normal and diabetic, of the individual amino-acids.

TABLE 1.—Analysis of 100 Grams Ox Meat with Respiratory Quotients

Substance	In 100 Gm. Meat gm.	Respiratory Quotient	
		Normal	Diabetic
Glycocoll	2.06	1.00	*
Alanin	3.72	0.83	*
Valin	0.81	0.75	
Leucin	11.65	0.73	
Prolin	5.82	0.82	0.60
Phenylalanin	3.15	0.87	
Aspartic acid	4.51	1.17	†
Glutamic acid	15.49	1.00	1.00
Serin	?	....	
Tyrosin	2.20	0.89	
Arginin	7.47	0.73	0.40
Histidin	1.76	0.90	
Lysin	7.59	0.71	
Ammonia	1.07		
Tryptophan	Present	0.87	
Total	67.30		

* R. Q. depressed below that of fat if glycocoll or alanin be ingested.
† R. Q. increased above that of fat if aspartic acid be given.

A glance at the above table shows how the respiratory quotient of 0.801 for protein is based on the sum of the results of the oxidation of many different substances, and also that the respiratory quotients usually tend to fall when certain of the amino-acids are converted into sugar.

A clear idea of this fall in the respiratory quotient can only be obtained if the respiratory metabolism of those amino-acids which are convertible into glucose is contrasted, the normal with the diabetic condition.

It will be noted in the foregoing table that only 67 per cent. of the ox protein was recovered as amino-acids. This is explained by the deficiency in the method; for Osborne and Jones[6] have analyzed a specially prepared mixture containing known quantities of a large number of amino-acids and have recovered only 66 per cent. of the substances present. As regards those amino-acids which are convertible into glucose, the following percentages were recovered from the mixture: Alanin, 46 per cent., prolin 73 per cent., aspartic acid, 42.5 per cent., glutamic acid 69 per cent., arginin 65 per cent. If one assumes that the quantity of glycocoll is at least double that found,

6. Osborne and Jones: Am. Jour. Physiol., 1910, xxvi, 325.

one arrives at values from which one may compute the quantity of sugar which should in theory arise from these acids. This appears in Table 2.

Since the 100 gm. of the ox muscle analyzed contained 16.18 gm. of nitrogen, the D:N equals 2.75:1.

TABLE 2.—Calculation Showing the Origin of Glucose from Protein

Substance	Osborne	Recalculated	Glucose
Glycocoll	2.06	4.0	3.2
Alanin	3.72	8.1	8.2
Aspartic acid	4.51	10.6	7.2
Glutamic acid	15.49	22.3	13.6
Prolin	5.82	8.0	6.3
Arginin	7.47	11.5	5.9
		64.5	44.4

TABLE 3.—Respiratory Exchange in the Normal and Diabetic Condition of Six Amino-Acids, as they are Contained in 100 Gm. of Ox Meat, and which are Convertible into 44.4 Gm. of Glucose, D: N = 2.75

Substance	Grams	Normal		Diabetic			
				Oxygen		Carbon Dioxid	
		Oxygen gm.	Carbon Dioxid gm.	Absorbed gm.	Eliminated in Reaction gm.	Absorbed in Reaction gm.	Eliminated gm.
Glycocoll ...	4.0	2.56	3.52	.....	0.85	1.17	
Alanin	8.1	8.75	10.01	0.0	.....	2.00	
Aspartic acid	10.6	7.65	12.27	0.0	.....	....	1.75
Glutamic acid	22.3	21.85	30.04	7.30	.....	....	10.03
Prolin	8.0	12.25	13.77	5.57	.....	....	4.59
Arginin	11.5	11.63	11.63	5.32	.....	....	2.91
				18.19	0.85	3.17	19.28
				0.85	....	....	3.17
	64.5	64.69	81.24	17.34			16.11
R. Q.		0.915		0.675			

When the D:N ratio is 3.65, 59 gm. of glucose, or 14.6 gm. more than the quantity above estimated, are eliminated in the urine when 100 gm. of protein are destroyed. These 14.6 gm. represent an additional amount of glucose whose origin is unexplained and which is equal to 24 per cent. of the total maximal production. Such sources of sugar might be cystin, which if all the sulphur in protein were in that form

might at most yield 2 gm. of glucose and serin whose solubility has prevented any accuracy of determination.

Having determined the approximate quantities of the various sugar yielding amino-acids, one may now compute the difference between their oxidation normally and in the diabetic. This is shown in Table 3.

This table signifies that when glycocoll, alanin, aspartic acid, glutamic acid, prolin and arginin, together aggregating nearly two-thirds by weight of the protein complex, are oxidized in the normal organism in the proportion in which they may exist in meat, the respiratory quotient is 0.915, whereas if 44.4 gm. of glucose is formed from them the respiratory quotient sinks to only 0.675.

Of those amino-acids which do not yield glucose, three, valin, leucin and lysin, which together aggregate 20 gm. according to Osborne's (uncorrected) analysis of 100 gm. of meat, have respiratory quotients of 0.75, 0.73 and 0.71, respectively, whereas three others, phenylalanin, tyrosin and histidin, together amounting to only 7.1 gm., yield respiratory quotients of 0.87, 0.89 and 0.90. Furthermore, the 1.07 gm. of ammonia liberated would tend to reduce the quotient through urea formation. It is therefore obvious that the respiratory quotient for protein in diabetes is made up predominately of the oxidation of the remnants of the sugar forming amino-acids and from the oxidation of other amino-acids having in the main respiratory quotients of 0.75 to 0.71. As actually calculated, the above named mixture of non-sugar producing amino-acids would yield 48.25 gm. of CO_2 and require 45.86 gm. of oxygen for oxidation, showing a respiratory quotient of 0.76.

The aggregate quotient of the non-sugar forming amino-acids as set forth above may be indirectly obtained by deducting the estimated respiratory exchange of the sugar-forming amino-acids from that of the total involved in the normal oxidation of 100 gm. of ox protein, as shown in Table 4.

TABLE 4.—Aggregate Quotient of Non-Sugar Forming Amino-Acids

	Oxyen gm.	Carbon Dioxid gm.	Resp. Quot.
Normal oxidation of 100 grams of beef protein	138.18	152.17	0.801
Estimated oxidation of the sugar forming amino-acids	64.69	81.24	0.915
	73.49	70.93	
Add CO_2 for urea formation from 1.07 gm. NH_3	.....	1.39	
Estimated oxidation of non-sugar forming amino-acids	73.49	72.32	0.716

Although the last respiratory quotient 0.716 closely approximates that of leucin (0.73) and lysin (0.71), the dominant non-sugar forming amino-acids, it is evident that the influence of the other non-sugar

forming amino-acids would tend to raise the quotient to a higher level, to 0.76 in the before mentioned calculation. Therefore, the present figures can only be regarded as an attempted solution of the problem rather than as a precise analysis.

When the mixture of six sugar-forming amino-acids, aggregating 64.5 gm., is normally oxidized

$$O_2 = 64.69 \text{ gm. and } CO_2 = 81.24 \text{ gm.}$$

and when it is converted into 44.4 gm. of glucose

$$O_2 = 17.34 \text{ gm. and } CO_2 = 16.11 \text{ gm.}$$

the difference between these two sets of figures will represent the quantities of respiratory gases which would not be involved in the respiratory exchange in diabetes and would amount to

$$O_2 = 47.35 \text{ gm. and } CO_2 = 65.13 \text{ gm.}$$

If one takes the grams of respired gases in the normal combustion of 100 grams of protein as given by Loewy, and deducts from these the quantity not eliminated according to the above computation, one arrives at the following results for the diabetic respiratory quotient:

TABLE 5.—PROTEIN RESPIRATORY QUOTIENT WITH D:N = 2.75

	Oxygen gm.	Carbon Dioxid gm.
Normal oxidation 100 grams beef protein...............	138.18	152.17
Deduct for intermediary production of 44.4 grams of glucose	47.35	65.13
	90.83	87.04

R. Q. = 0.697.

Proceeding now to the consideration of the cases of diabetes in which the D:N is 3.65, calculations have been made the relations of which may be thus presented:

TABLE 6.—PROTEIN RESPIRATORY QUOTIENT WITH D:N = 3.65

	Oxygen gm.	Carbon Dioxid gm.
(1). Normal oxidation of 100 grams of beef protein......	138.18	152.17
Deduction, if 16.28 grams N $\times$ 3.65 = 59.41 glucose.....	63.38	87.15
	74.80	65.02

R. Q. = 0.632.

The respiratory quotient for fat is 0.707, and since fat forms the main recourse of the diabetic, the respiratory quotient will be found nearer to that of fat than to 0.632 for protein. Thus, in a diabetic dog with a D:N ratio of 3.54 in which 23 per cent. of the total heat production was derived from protein and 77 per cent. from fat, the

respiratory quotient was 0.687, the non-protein respiratory quotient being 0.704, which closely approximates that of fat. In the case of a diabetic patient with a low protein metabolism whose urinary D:N was 3.6, Du Bois has found during a three hour period a respiratory quotient of 0.697. In another diabetic man with approximately the same D:N ratio but whose protein metabolism was higher (13 per cent. of the total energy) the R. Q. was 0.691.

Magnus-Levy[7] has called attention to a possible reduction in the respiratory quotient when beta-oxybutyric acid is formed from fat. He estimates that the maximal quantity of beta-oxybutyric acid derivable from 100 gm. of fat is 36 gm. Under these circumstances, the respiratory quotient for fat would be reduced from 0.707 to 0.669. The case is not so simple, however, for if the 36 gm. of acid formed neutralized sodium bicarbonate, 15.23 gm. of carbon dioxid would be eliminated.

These relations are shown in Table 7:

TABLE 7.—Theoretical Respiratory Quotient with Beta-Oxybutyric Acid Formed from Fat

	Oxygen Liters	Carbon Dioxid Liters	R. Q.
100 gm. fat	201.9	142.73	0.707
36 gm. beta-oxybutyric acid	34.85	30.96	0.889
	167.05	111.77	0.669
Add for 15.23 gm. CO_2 from $NaHCO_3$		7.74	
Possible end result	167.05	119.51	0.715

Since other bases than sodium bicarbonate may be used for the neutralization of beta-oxybutyric acid, it is apparent that the exact determination of the theoretical respiratory quotient when this acid is produced in large amounts in human diabetes is at present impossible.

This discussion has been prepared in order to further the understanding of a forthcoming description of metabolism in diabetes mellitus.

7. Magnus-Levy: Ztschr. f. klin. Med., 1905, lvi, 83.

CLINICAL CALORIMETRY

NINTH PAPER

FURTHER MEASUREMENTS OF THE SURFACE AREA OF ADULTS AND CHILDREN *

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In paper 5[1] of this series a method was described by means of which it was possible to determine the surface area of living subjects. On the basis of the measurements of five persons of widely varying body shapes, a formula was devised by Mr. Delafield Du Bois which gave an average error of only 1.7 per cent. when applied to the persons measured. The number of subjects was rather small and it has seemed best to continue the work and apply the formula to persons of unusual shapes.

Since the publication of the previous paper, in which the literature was reviewed, a number of references have come to light largely through the attention of Dr. Francis G. Benedict of the Nutrition Laboratory of Boston. The work of Sicheff[2] is of considerable importance. Working in Gundobin's clinic he applied the methods used by Meeh to twenty-four children from the ages of 1 day to 15 years, and to one adult. He found the surface area proportional to the two third power of the weight, but the average constant by which this should be multiplied is 10.7, according to his figures, instead of Meeh's figure of 11.9. In the case of the adult the constant would be 8.8, which is at such variance with the results of other investigators that it would seem as if some error must have crept into the calculations in this one case.

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1. Paper 5, Clinical Calorimetry, THE ARCHIVES INT. MED., 1915, xv, 868.

2. Sicheff (Ssytscheff), A. I.: Measurement of the Volume and the Surface of the Body of Children According to Age, Inaug. Dissert., Petrograd, 1902. The tables are given in Gundobin, Die Besonderheiten des Kindesalters, Berlin, 1912. We are indebted to Dr. Benedict for permission to consult the translation of the original article in the Nutrition Laboratory.

Variot and Saint Albin[3] have measured the surface of a number of children using pieces of tin foil, and Maurel[4] has worked out the relationship of the thorax dimension to surface area. Letulle and Pompilian[5] in 1906 used a method of determining surface area somewhat similar to the formula adopted by D. Du Bois nine years later. They consider that the surface of the body consists of a number of trapezoids, one covering the upper arm, one the forearm, one the hand, one for each finger, etc. They calculate the area of each trapezoid from the length of the part and the circumference at the two borders which form the sides of the figure. The errors inherent in this method become evident when one looks at the factors used in the "Linear Formula" of D. Du Bois. It is necessary to correct the average length and breadth of each part by a factor to obtain the true surface. Lassabliere[6] measured the surface of a large number of children by marking out the skin in geometrical patterns and determining the area by means of a perimeter. He found the skin area proportional to 10.5 $Wt.^2$ or to 0.92 $Ht.^2$ or to 2.3 $Perim.^2$, Wt. being the kilograms of body weight, Ht. the height in centimeters and Perim. the circumference of the thorax at the level of the nipples.

INDIVIDUALS MEASURED

Anna M.—This was the cadaver of a child 21 months old, weighed and measured about two hours after death. The subject was small for her age and had suffered from rachitis, the epiphyses at the wrists were large and the thorax was pigeon-breasted, being narrow and very deep anteroposteriorly. The child had pertussis and developed a fatal pneumonia.

Fabian R. S., aged 12 years, 10 months, an unusually well formed boy with no signs of puberty as yet. He was muscular and rather short for his age. He served as the subject for one of the calorimeter experiments described in Paper 12.

Gerald S., 18 years old, tall and much emaciated. He was a diabetes patient and a complete description of his case is to be found in Paper 17. He was given the Allen fasting treatment from November 11 to 19, and the measurements were taken December 1 after he had been on a maintenance diet for about a week. His weight at one time dropped to 38.7 kg., but increased to 45.25 kg. as a result of food ingestion, and also on account of an invisible edema.

ERROR IN PREVIOUS PAPER

A brief preliminary note about the measurements of Gerald S. was given at the end of Paper 5[1] of this series. The discrepancy between the calculated

3. Variot and Saint Albin: La mensuration de l'aitre cutanée des jeunes enfants par l'enveloppement avec des feulles d'etain, Bull. Soc. de pediat. de Paris, 1903, v, 307.

4. Maurel, E.: Adaption de la section thoracique a la surface cutanée par rapport an poids, depuis la maissance jusqu'a l'age adult, Compt. rend. Soc. de biol., 1904, lvi, 980.

5. Letulle and Pompilian: Methode de recherche applicable a l'étude de la nutrition, Rev. Soc. scient. d'hyg. aliment., 1906, iii, 708.

6. Lassabliere, P.: Evaluation de la surface cutanée chez le jenne enfant. Compt rend. Soc. de biol., 1910, 339.

TABLE 1.—Measurements Used in Formula

	Anna M., Cm.	Fabian S., Cm.	Gerald S., Cm.	Emma W., May 8, Cm.	Emma W., May 13 and 17, Cm.	R. H. S. June 18, Cm.	Robert L., Cm.	Harry J., Right Side, Cm.	Harry J., Left Side, Cm.
A—Around vertex and chin	49.1	61.5	62.2	64.4	....	67.0	67.9	64.6	....
B—Around occiput and forehead	44.0	54.4	51.2	55.0	....	58.0	57.2	55.5	....
F—Acromion to lower border of radius	22.9	49.5	65.5	58.6	....	67.7	54.6	59.4	57.7
G—Circumference of arm at upper border of axilla	10.5	20.5	20.0	27.5	27.0	26.3	33.6	32.2	34.5
H—Largest circumference of forearm	11.9	19.7	21.0	23.4	23.8	25.4	26.2	28.2	29.0
I—Smallest circumference of forearm	9.1	13.3	15.0	14.3	14.8	16.7	16.1	16.2	16.5
J—Lower posterior border of radius to tip of second finger	8.7	16.4	19.8	17.5	....	21.9	19.2	17.9	....
K—Circumference of hand at knuckles	8.6	17.4	19.9	17.6	....	20.6	20.6	20.2	....
L—Suprasternal notch to upper border of pubes	26.0	46.0	51.3	51.3	....	58.6	56.7	50.0	....
M—Circumference of abdomen at umbilicus	35.1	56.8	64.7	71.9	70.1	69.8	92.6	78.2	....
N—Circumference of thorax at nipples in male and just above breasts in female	38.6	66.2	78.5	81.0	83.0	85.9	100.6	96.2	....
O—Superior border of great trochanter to lower border of patella	16.0	37.8	44.7	45.7	....	50.3	47.5	....	....
W—Superior border of pubes to lower border of patella	14.4	33.7	44.9	41.7	....	46.3	....	....	....
P—Circumference of thigh at perineum	20.6	41.2	41.4	53.7	55.3	48.3	52.7	....	....
Q—Circumference of hips and buttocks at level of trochanters	39.5	69.7	76.5	93.8	93.2	87.0	94.9	....	....
R—Sole of foot to lower border of patella	16.0	36.4	48.3	45.3	....	53.1	....	....	....
S—Circumference at lower border of patella	14.2	27.6	31.7	32.0	34.8	34.8	....	....	....
T—Length of foot, including great toe	10.5	21.4	26.0	23.3	....	27.5	....	....	....
U—Circumference at base of little toe	8.9	19.8	21.2	21.3	....	21.7	....	....	....
V—Smallest circumference of ankle	9.9	16.5	17.8	20.3	....	23.8	....	....	....

and measured areas of the thorax was so much greater than in any other case that an error was suspected. It became apparent that the recorded length of the thorax was 10 cm. too short. This measurement L. had been determined by subtracting the distance from foot to upper border of the pubes from III, the distance from foot to suprasternal notch. The recorded measurements in the case of Gerald S. from the sole of the foot were as follows: "To suprasternal notch, 134.5 cm."; to outer end of clavicle, 145.8; to upper border of axilla, 136.2; to tip of ensiform, 125.0; to the nipples, 134.3; height, 171.8. It was evident that the suprasternal notch must have been more than 0.2 cm. above the nipples. To find its correct position the measurements of the five subjects whose shape was nearest to that of Gerald S. were tabulated and the average percentage of the height shared by the distance between suprasternal

TABLE 2.—Measurements Not Used in Formula

	Anna M.	Fabian S.	Gerald S.	Emma W. May 3	R. H. S. June 18
I—Weight, Kg.	6.27	32.74	45.25	57.62	68.00
	Cm.	Cm.	Cm.	Cm.	Cm.
II—Height or length	78.2	141.5	171.8	164.8	184.2
III—Sole of foot to suprasternal notch	54.8	114.7	144.5	135.7	152.2
IV—Sole of foot to nipples	50.4	107.0	134.3	123.9	140.2
V—Sole of foot to upper border of axilla	53.2	109.8	136.2	127.9	145.8
VI—Sole of foot to tip of ensiform	45.6	100.2	125.0	117.5	129.8
VII—Sole of foot to superior border of great trochanter	30.2	73.7	93.0	88.5	108.1
VIII—Sole of foot to perineum	26.6	64.2	86.0	76.4	92.1
IX—Circumference of thorax at tip of ensiform	41.2	65.0	76.5	74.0	78.8
X—Tip of second finger to upper border of axilla	—	.....	67.5	.....	.....
XI—Tip of second finger to tip of olecranon	18.6	37.9	46.9	43.3	51.9
XII—Tip of second finger to metacarpophalangeal joint	4.9	9.8	10.8	10.1	12.3
XIII—Tip of olecranon to lower border of radius	9.8	22.3	28.0	26.0	31.5
XIV—Tip of olecranon to acromion process	13.0	28.0	37.5	32.8	37.7
XV—Circumference of arm at insertion of deltoid	10.4	19.4	18.7	26.0	25.6
XVI—Circumference of arm at belly of biceps	10.6	19.1	18.3	23.8	25.1
XVII—Circumference of thigh half way between anterior superior spine of ilium and lower border of patella	17.8	39.2	37.6	52.2	47.0
XVIII—Largest circumference of calf	13.0	26.6	27.2	35.0	31.0
XIX—Circumference of foot at heel	11.9	26.5	30.2	29.7	31.5
XX—From back of neck around superior maxilla	31.8	42.5	43.5	45.0	43.3
XXI—Around neck just below larynx	17.5	29.0	30.8	33.5	36.5
XXII—Around shoulders at level of heads of humeri	39.8	73.5	87.4	91.0	108.6

notch and various neighboring parts was calculated. The projected location of the suprasternal notch in Gerald's case according to three different methods was 145.6, 142.4 and 144.2. The measurement 144.5 was adopted since it seemed probable that the error had consisted in recording a 3 instead of a 4. Unfortunately the subject had died before the error was suspected and could not be measured again.

Emma W., 26 years old, a sculptor's model. She was well proportioned, slightly above the average height and was neither fat nor thin. She had always been athletic and her muscles were well developed.

R. H. S., 21½ years old. An unusually tall and thin man who had lost about 5 pounds during the past year. For three days before his first measure-

ment an attempt was made to reduce his weight still further. He was kept for two days on a diet low in carbohydrates and salt. On the morning he was measured he took a light breakfast and played tennis for one and one half hours, drinking no water after the exercise.

Robert L., 43 years old. Five years previously he had lost both legs in a railroad accident. The right limb was cut off 50.5 cm. below the superior border of the great trochanter, the left 25.5 cm. below the same point. Both stumps were atrophied from disuse. His face, trunk and arms were fat.

Harry J., 34 years old, colored, usually called "Rubber tires" from the wheels on which he propelled himself with the velocity of a bicycle. His legs had been cut off in a railroad accident when he was only 6 years old. As a result of his deformity he had developed a form which reminded one of a hermit crab. The shoulders and arms were very large and powerful, the hips were those of an undeveloped boy, the stumps were atrophic. The left leg was cut off at the knee, the right about half way up the thigh. Six years previous to examination he had a stroke of apoplexy and the right side of the body was paralyzed, but was now spastic with some power of movement. As a result of this he propelled himself on his wheels and lifted himself about entirely with his left arm, which was unusually strong. He had no superfluous fat on his body.

METHODS USED

The area of the molds was determined by the method of printing on photographic paper and weighing described in Paper 5. In some of the cases, however, the molds were made by new methods, although the paper strip method previously described proved the most accurate and was used in all cases except when specifically noted. The cadaver of the baby, Anna M., was dressed in tight fitting clothing and melted paraffin applied to the whole surface. In the case of Fabian S. the tight fitting underclothing was covered with strips of surgeons' adhesive plaster and over this melted paraffin was painted. This same method was used in the first mold of Emma W. on May 3. It was noted that in both these cases it was comparatively easy to cut the mold open, while with the paper strip method it was hard to get even small probe-pointed scissors between the mold and the skin. This led to the suspicion that the adhesive plaster stretched, so the measurement of four of the parts was repeated with Emma W. Molds of the arm and leg were taken by the paper strip method on May 13, and of the trunk and thigh on May 17, measurements of the parts being made on the same day. The weight on May 3 was 58.09 kg.; on May 13 57.22; on May 17, 57.62 kg. It will be seen in Table 3 that the paper method results were 6.5 per cent. smaller for the arms, 8.6 per cent. smaller for the thighs, 4.5 per cent. smaller for the legs and 1.6 per cent. larger for the trunk. When the totals for the four parts are compared, the paper results are 3.3 per cent. lower, and it may be concluded that the data obtained by the adhesive plaster method in the case of Fabian S. are about 3.3 per cent. too high and therefore should be excluded from the averages.

In all of these subjects the left upper and lower extremities were not included in the molds or in the measurements. In the case of Harry J., molds were made of the trunk and thighs alone, and with Robert L. the mold of the head was omitted.

The measurements were made in the manner described in the previous paper and the same letters and numbers applied to them. In the previous work the measurement F was obtained by adding XIII and XIV, the distance from the tip of the olecranon to the lower border of the radius and from the olecranon to the outer end of the clavicle. These measurements had been made with the arm bent and their sum averages 9.5 per cent. larger than the measurement from acromial process to lower border of the radius with the arm straight. Therefore, in using the formula the measurements should be made with the arm bent or else the factor 0.611 used instead of 0.558.

TABLE 3.—COMPARISON OF AREAS OF PARTS OF BODY AS—

Name	Head			Arms			Hands		
	Measured	Formula	Error, %	Measured	Formula	Error, %	Measured	Formula	Error, %
Anna M.	610	665	+9	486	403	—17	214	166	—23
F. R. S.*	(1087)*	1081	(—0.5)	(1620)*	1478	(— 9)	640	628	— 2
Gerald S.	950	978	+8	2152	2047	— 5	876	875	— 0
Emma W.*	(1079)	1091	(+1)	(2402)*	2132	(—11)	806	688	—15
Emma W.	......	.....	......	2252	2145	— 5	...	...	....
R. H. S.	1208	1197	—1	2778	2584	— 7	891	1002	+12
Robert L.	......	1196	......	2672	2318	—14	956	878	— 8
Harry J.	......	1104	......	......	2558	......	...	...	....

* Measured by adhesive plaster method; results average 8.8 per cent. too high.

ACCURACY OF METHOD

In order to give the method of measurement of the surface area a severe test, molds were made of a bowling ball, a perfect sphere with an average diameter of 21.78 cm. and a calculated surface of 0.1490 square meters. The first mold was made by covering the ball with two layers of surgeon's gauze, pasting strips of paper over this, cutting off the mold and coating the inside with paraffin. The area of this mold was found to be 0.1566 square meters, or 5.1 per cent. too large. A second mold was made with greater care. Only one thickness of gauze was used and this was drawn over the ball like a bag, the excess being trimmed off. The paper strips were pasted very tight and the paraffin omitted. The area of the second mold was 0.1488 square meters, or

0.13 per cent. lower than the theoretical surface area. This shows that the method is accurate if the paper be applied very tightly in the manner always used by us, but that if the strips be applied at all loosely, or if a material such as adhesive plaster be used, there may be a plus error of 3 to 5 per cent.

One criticism of the linear formula which has been made is that it would be difficult for two observers to obtain concordant results on the same individual. To test this point a man 182.8 cm. tall, weighing 87.08 kg., was measured by two of the staff independently and the surface calculated according to the "Linear Formula." The first result was 2.0733 square meters, the second 2.0798, the difference being 0.3 per cent. Another subject was measured independently by two physicians, one of whom had never seen the method applied, and the results agreed within 0.5 per cent. This is probably closer agreement

—ACTUALLY MEASURED AND AS CALCULATED FROM FORMULAS

Trunk			Thighs			Legs			Feet		
Measured	Formula	Error, %	Measured	Formula	Error, %	Measured	Formula	Error, %	Measured	Formula	Error, %
1855	1347	− 1	478	488	+ 2	340	318	− 7	216	205	−5
(4118)*	3978	(− 3)	(2166)*	2130	(− 2)	(1456)*	1407	(− 3)	(834)*	808	(−3)
5003	5165	+ 3	3002	2677	−11	1876	2144	+14	1042	1055	+1
(5526)*	5482	(− 1)	(3608)*	3424	(− 5)	(2392)*	2030	(−15)	(1064)*	1082	(−5)
5618	5522	− 2	3324	3448	+ 4	2288	2207	− 4			
6064	5867	− 3	3155	3457	+ 9	2634	2587	− 2	1251	1301	+4
6897	7701	+12	1755	1781	+ 1						
6599	6130	− 7	794 1196	Right Left							

than would often be found, since measurements of the same part made by one man sometimes differ by 5 per cent. There is no factor except a difference in the tension of the tape which would throw the error in one direction more often than the other.

DISCUSSION OF RESULTS

Tables 1 and 2 give the linear measurements, and Tables 3 and 4 the results of the determinations of the surface area. The individual parts show a somewhat greater divergence between the area as determined by formula and as actually measured than in the former paper, but this was to be expected. The total results are all that could be desired. In the cases of Gerald S. and R. H. S. the errors in the

formula are 0.3 and 0.1 per cent, respectively. With Anna M. and with Emma W. as measured by the paper method, — 2.9 and — 2.0 per cent. The average error for these four subjects is 1.3 per cent. Fabian S. shows an apparent error of 3.5 per cent. when measured by the adhesive plaster method. This would be reduced to — 0.2 per cent if we made the correction for the average plus error of 3.3 per cent. in the adhesive method.

TABLE 4.—SUMMARY

Name	Surface Area		Error, %	Surface Area, Meeh's Formula	Error, %	Correct Constant Meeh's Formula	Age, Yrs.	Weight, Kg.	Height, Cm.
	Measured	Linear Formula							
Anna M.	0.3699	0.3592	—2.9	0.405*	+ 9.3	10.9	2	6.27	78.2
F. R. S.	(1.1869)†	1.1455	(—3.5)	1.260	(+ 6.2)	(11.6)	12	32.74	141.5
Gerald S.	1.4901	1.4941	+0.3	1.563	+ 4.9	11.7	17	45.25	171.8
Emma W.	(1.6897)†	1.5874	(—6.0)	.....	......	....	26	.....	.....
Emma W.	1.6451	1.6128	—2.0	1.837	+11.6	11.0	26	57.62	164.8
R. H. S.	1.7981	1.7995	+0.1	1.949	+ 8.4	11.4	21	63.00	184.2
Robert L.	1.4299	1.4692	+2.7	1.960	+37.0	....	..	63.81	.....
Harry J.	......	1.3054	.....	1.800	+38.0	....	..	55.92	.....

* Constant used for Meeh's formula for the baby = 11.9, for adults 12.3.
† Measured by adhesive plaster method; results average 3.3 per cent. too high.

SUMMARY AND CONCLUSIONS

The so-called "Linear Formula" for the estimation of the surface area has been satisfactorily tested on four new subjects of varying size and shape. In addition, partial measurements of two legless men have been made. The average error in the formula when applied to the four subjects was 1.3 per cent. Two of the subjects were children and in these cases the error in the formula was under 3 per cent. Since the youngest was about 2 years old it does not seem advisable to use the formula for babies under this age until the factors have been tested by the measurements of infants.

In conclusion we wish to thank Dr. A. L. Meyer and Mr. G. F. Soderstrom for their aid in making the molds and measuring the subjects.

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CLINICAL CALORIMETRY

TENTH PAPER

A FORMULA TO ESTIMATE THE APPROXIMATE SURFACE AREA IF HEIGHT AND WEIGHT BE KNOWN *

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Since the publication of Paper 5 of this series the so-called "Linear Formula" has been used in the study of a large number of individuals. Practically all of the subjects of respiration experiments in the Sage calorimeter have been measured in this way, and in addition Means[1] of Boston has used it as a factor in determining his normal base line of metabolism and the extent of the pathological variations. Means has found that the range of normal variation from the average is smaller and that the apparent depression of metabolism in obesity is much less marked when the linear formula, instead of Meeh's formula, is used to determine surface area.

The accuracy of the linear formula has been shown in Paper 9 of this series. In order to correct the slight error in the factor for the arms, and also in order to clear up a few points in the measurements which may cause confusion, it seems best to repeat the formula and show the bony landmarks by diagram (Fig. 1). Some difficulty has been experienced in locating the superior border of the great trochanter in fat subjects. This landmark is the starting point of the measurement "O" which represents the length of the thighs. If we employ another factor we can use the new measurement "W," the distance from lower border of the patella to the upper border of the pubes, a point already located in the measurement "L." In taking this measurement, however, one must be careful to have the legs straight and the knees, heels and great toes touching. It is better to take all measurements from a footboard with the subject lying down,[2] determining distance from soles of feet to lower border of patella, to upper border of

* Submitted for publication Feb. 4, 1916.
* From the Russell Sage Institute of Pathology, in Affiliation with the Second Medical Division of Bellevue Hospital.

1. Means, J. H.: Studies of the Basal Metabolism in Obesity and Pituitary Disease, Jour. Med. Research, 1915, xxxii, 121; Basal Metabolism and Body Surface, Jour. Biol. Chem., 1915, xxi, 263.

2. This is especially important with obsese patients.

pubes, to suprasternal notch and to top of the head.[3] In Table 1 a comparison is made of the old and new formulas for determining the surface of the thighs. It is seen that the average error is the same.

In the literature of the work on respiratory metabolism it has been customary to give only the age, weight and height. If, therefore, we

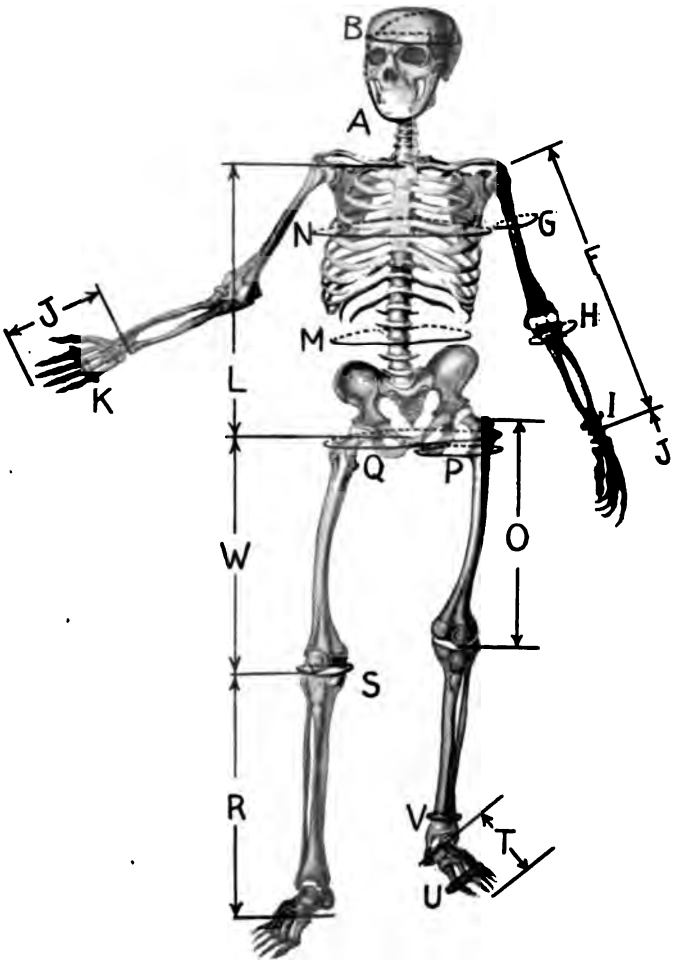

Fig. 1.—Measurements used in "Linear Formula."

are to recalculate previous work in an effort to get more accurate results than are furnished by Meeh's formula we must content ourselves with calculations based on height and weight. A formula such as Meeh's, based on weight alone, can easily give an error of 15 to 20 per cent.,

3. Dr. F. G. Benedict of Boston has called our attention to the fact that this determines the length rather than the height. We have found that as a rule the length is 1 or 2 centimeters greater than the height, but we must remember that height varies 1 to 3 centimeters during the day.

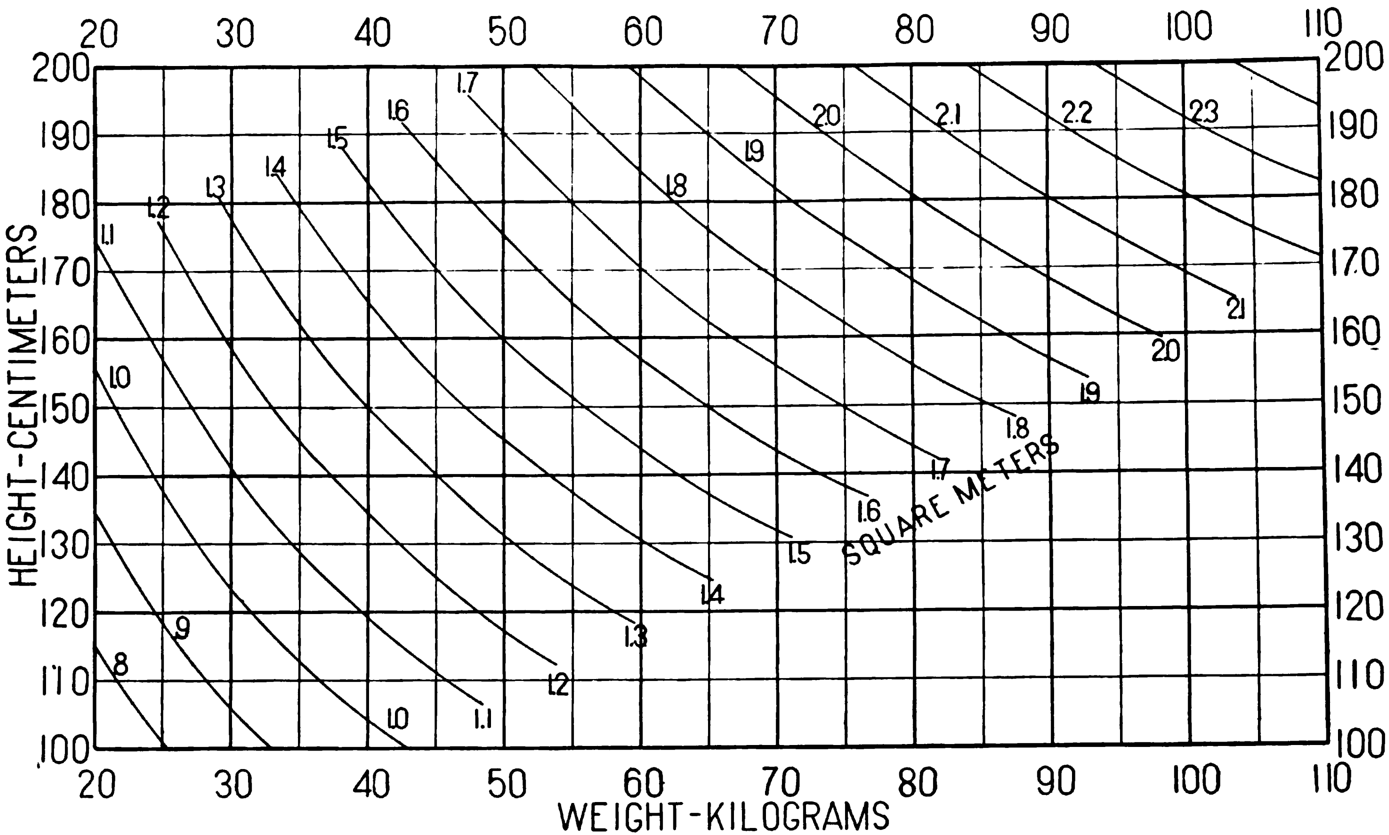

Fig. 2.—Chart for determining surface area of man in square meters from weight in kilograms (Wt.) and height in centimeters (Ht.) according to the formula: Area (Sq. Cm.) $= Wt.^{0.425} \times Ht.^{0.725} \times 71.84$.

but this error is greatly reduced by taking the height into consideration. With people of very unusual body shape there does not seem to be any accurate method simpler than the linear formula with its nineteen measurements. The reason why a consideration of the height does not entirely correct the calculations based on weight becomes apparent when we consider the circumference of the body at various levels. For instance, in the case of R. H. H. the average circumference of the legs was 30.0 cm. and of the thighs 43.9 cm. An increase of 10 cm. in the length below the knees would mean an increase of 600 sq. cm. in surface area, but if the length of the thighs were increased 10 cm. it would mean a gain of 878 sq. cm. Variations in the arms would not affect the height at all.

TABLE 1.—Comparison of Old and New Formulas for Determining Surface Areas of Thighs

Name	Thigh Measurement* "O" Cm.	Thigh Measurement* "W" Cm.	Surface Thighs as Meas., Sq. Cm.	Surface Calc. O(P+Q) 0.508	Error, %	Surface Calc. W(P+Q) 0.552	Error, %
Benny L.	26.4	22.4	1284	1294	+1	1195	− 7
Morris S.	41.7	33.8	3022	3207	+6	3251	+ 7
R. H. H.	47.0	46.0	3712	3512	−5	3745	+ 1
E. F. D. B.	46.3	46.3	3820	3655	−4	3961	+ 4
Mrs. McK.	40.0	32.2	3500	3594	+3	3152	−11
Anna M.	16.0	14.4	478	488	+2	479	+ 0
Gerald S.	44.7	44.9	3002	2677	−11	2927	− 3
Emma W.	45.7	41.7	3324	3448	+4	3425	+ 3
R. H. S.	50.3	46.3	3175	3457	+9	3464	+ 9
Average	....	....	....	....	±5	....	± 5

* Old measurement "O," superior border of great trochanter to lower border of patella. New measurement "W," superior border of pubes to lower border of patella.

A formula to express surface area must naturally be a bi-dimensional formula, as surface involves two dimensions. If we assume that weight is proportional to volume, it is obvious that three dimensions are involved in any expression for weight. Height is, of course, a single dimension. If we attempt to construct a formula for surface area (A) based on weight (W) and height (H), it is obvious that a simple formula such as $A = W \times H \times C$ (C being a constant depending on the units used and the subject to which the formula is to apply) is not logical. In this formula one side, A, is bidimensional and the other side, $W \times H \times C$, involves four dimensions, three from W and one from H. If W is tridimensional, it is obvious that the cube

root of W ($=\sqrt[3]{W}$ or $W^{1/3}$) is undimensional and a formula $A = W^{1/3} \times H \times C$ is logical in that it is bidimensional on both sides. Another bidimensional expression involving W and H would be the square root of $W \times H$ ($\sqrt{W \times H}$ or $W^{1/2} \times H^{1/2}$) because $W \times H$, being four-dimensional, is reduced to a bidimensional expression on taking the square root. A formula based on this method of reduction would be $A = W^{1/2} \times H^{1/2} \times C$.

TABLE 2.—Measurements and Constants for Linear Formula (Measurements Taken with Subject Lying on a Flat Surface)

Head: AB 0.308.
- A—Around vertex and point of chin.
- B—Coronal circumference around occiput and forehead, just above eyebrows.

Arms: F(G + H + I) 0.611.*
- F—Tip of acromial process to lower border of radius, measured with forearm extended.
- G—Circumference at level of upper border of axilla.
- H—Largest circumference of forearm (just below elbow).
- I—Smallest circumference of forearm (just above head of ulna).

Hands: JK 2.22.
- J—Lower posterior border of radius to tip of second finger.
- K—Circumference of open hand at the meta-carpo-phalangeal joints.

Trunk (Including neck and external genitals in the male, breasts in female): L(M + N) 0.703.
- L—Suprasternal notch to upper border of pubes.
- M—Circumference of abdomen at level of umbilicus.
- N—Circumference of thorax at level of nipples in the male and just above breasts in the female.

Thighs: O(P + Q) 0.508.
- O—Superior border of great trochanter to the lower border of the patella.
- P—Circumference of thigh just below the level of perineum.
- Q—Circumference of hips and buttocks at the level of the great trochanters.

Or:—Thighs: W(P + Q) 0.552.
- W—Upper border of pubes to lower border patella (measured with legs straight and feet pointed anteroposteriorly).
- P—As above.
- Q—As above.

Legs: RS 1.40.
- R—From sole of foot to lower border of patella.
- S—Circumference at level of lower border of patella.

Feet: T(U + V) 1.04.
- T—Length of foot including great toe.
- U—Circumference of foot at base of little toe.
- V—Smallest circumference of ankle (just above malleoli).

* Factor 0.558 if F is measured over olecranon with forearm flexed.

Note.—The constants for arms, thighs, etc., when multiplied by the measurements of one side give the surface area for both sides. To find total surface area add the seven parts.

TABLE 3.—COMPARISON OF VARIOUS FORMULAS

Name	Weight, Kg.	Height or Length, Cm.	Measured or Determined by Linear Formula, Area, Sq. Cm.	$\frac{\text{Area}}{\text{Ht.}\sqrt[3]{\text{Wt.}}}=\text{C}$		$\frac{\text{Area}}{\sqrt{\text{Ht.}\times\text{Wt.}}}=\text{C}$		$\frac{\text{Area}}{\text{Wt.}^{\frac{1}{2.35}}\times\text{Ht.}^{\frac{1}{1.38}}}=\text{C}$	
				Factor C	Variation from 25.6, %	Factor C	Variation from 167.2, %	Factor C	Variation from 71.84, %
Measured by Molds:									
Benny L.	24.2	110.3	8473	26.7	+4.3	164.0	—2.0	72.30	+0.7
Morris S.	64.0	164.3	16720	25.5	—0.5	163.0	—2.5	70.65	—1.6
R. H. H.	64.1	178.0	18375	25.8	+0.8	171.5	+2.6	73.22	+1.9
E. F. D. B. ..	74.1	179.2	19000	25.3	—1.2	164.7	—1.5	70.85	—1.3
Mrs. McK. ...	93.0	149.7	18592	27.2	+6.2	157.5	—5.8	71.70	—0.2
Gerald S.	45.2	171.8	14901	24.4	—4.7	169.2	+1.2	70.36	—2.0
Fab. S.	32.7	141.5	(11869)*	25.5	(—0.5)*	174.2	(+4.0)*	74.37	(+3.5)*
Anna M.	6.27	73.2	3699	27.4	+7.1	172.0	+3.0	75.54	+5.1
Emma W. ...	57.6	164.8	16451	25.8	+0.8	169.0	+1.1	72.56	+1.0
R. H. S.	63.0	184.2	17981	24.5	—4.3	167.0	0.0	70.56	—1.7
Average....	....	.....	.....	....	+3.3	.....	+2.2	.....	+1.7
Measured by Linear Formula									
Edw. B.	62.3	174.0	17270	25.0	—2.3	165.2	—1.2	70.75	—1.5
John K.	65.4	176.0	17610	24.9	—2.7	164.2	—1.7	70.83	—1.4
Alb. S.	66.4	162.2	16720	25.5	—0.5	161.0	—3.7	70.20	—2.3
Wm. S.	44.6	179.0	15450	23.7	—7.4	172.8	+3.3	71.53	—0.4
A. F. O.	69.6	179.4	17960	24.4	—4.7	160.5	—4.0	68.71	—4.4
Wm. A.	63.4	180.0	17940	24.9	—2.7	168.2	+0.6	71.22	—0.8
Mart. O.	44.0	166.8	14370	24.5	—4.3	167.5	+ .1	70.44	—1.9
Jos. U.	40.1	179.0	14520	23.7	—7.4	171.2	+2.3	70.36	—2.1
Wm. Shee....	63.8	171.0	16070	23.5	—8.2	154.8	—7.5	66.06	—8.0
Arthur V. ...	58.3	155.0	15560	25.8	+0.8	163.3	—2.4	73.02	+1.6
Armon W. ...	60.8	161.0	15500	23.6	—7.8	156.6	—6.4	67.96	—5.4
Annie T.	26.3	137.0	10460	25.6	0.0	174.0	+4.1	73.60	+2.4
Fred D.	49.3	157.0	13870	24.1	—5.8	157.2	—6.0	67.69	—5.7
Fred D.	40.0	157.0	12960	24.2	—5.5	163.5	—2.3	69.12	—3.8
Edw. T.	50.4	168.0	14830	23.4	—8.6	161.0	—3.7	68.27	—5.0
J. McE.	41.8	166.0	13260	23.1	—9.7	159.0	—4.8	66.67	—7.2
Bart D.	48.5	156.0	13850	25.3	—1.2	168.1	+0.5	71.62	—0.3
Burr Ph.	70.7	169.0	17390	24.9	—2.7	159.0	—4.8	69.01	—3.9
J. D. D. B. ...	34.5	152.8	12240	24.7	—3.5	168.6	+0.7	70.90	—1.3

TABLE 3.—(*Continued*)

Name	Weight, Kg.	Height or Length, Cm.	Measured or Determined by Linear Formula, Area, Sq. Cm.	$\frac{\text{Area}}{\text{Ht.}\sqrt[3]{\text{Wt.}}} = C$		$\frac{\text{Area}}{\sqrt{\text{Ht.} \times \text{Wt.}}} = C$		$\frac{\text{Area}}{\text{Wt.}^{\frac{1}{2.35}} \times \text{Ht.}^{\frac{1}{1.38}}} = C$	
				Factor C	Variation from 25.6, %	Factor C	Variation from 167.2, %	Factor C	Variation from 71.84, %
Ray M.	30.4	140.5	10840	24.8	−3.1	165.8	−0.8	70.42	−1.9
Harry B.	36.5	146.0	12320	25.4	−0.8	168.6	+0.8	72.01	+0.3
Harry K.	35.9	148.2	12240	25.0	−2.3	167.8	+0.2	71.30	−0.8
Arthur A. ...	30.6	146.6	11260	24.6	−3.9	167.0	−0.1	70.71	−1.6
Leslie B.	28.5	140.8	10600	24.5	−4.3	166.5	−0.5	70.00	−2.6
Peter N.	63.4	187.7	17950	24.0	−6.2	164.2	−1.8	69.09	−3.8
Max W.	73.2	173.7	18540	25.5	−0.5	164.5	−1.7	71.07	−1.1
Dan O'C.	60.0	167.0	16570	25.4	−0.8	165.7	−1.0	71.12	−1.0
Jack O'C. ...	31.4	162.8	12040	23.5	−8.2	168.2	+0.6	69.35	−3.5
A. F.	52.6	159.0	14870	25.0	−2.3	162.5	−2.9	69.95	−2.6
G. L.	79.2	175.5	20300	26.9	−5.1	172.2	+3.0	74.70	+4.0
F. C. G.	56.5	173.9	16440	24.7	−3.5	167.4	0.0	70.29	−2.1
L. M.	59.5	170.6	16340	24.6	−3.9	162.1	−3.0	69.30	−3.5
F. G. B.	87.1	182.8	20760	25.8	−0.8	164.5	−1.1	71.22	−0.9

* Measured by adhesive plaster method which gives results about 3.3 per cent. too high. The plus variations would be reduced by this amount.

Comparing the two formulas $A = W^{1/3} \times H \times C$ and $A = W^{1/2} H^{1/2} \times C$, it will be seen that they differ in the relative importance given to W and H. In the former W has less importance and H more importance than in the latter. Meeh's formula $A = W^{2/3} \times C$, failed because H was neglected entirely. Adding H to the formula makes it more nearly applicable to subjects of the same general shape but differing somewhat in relative dimensions, and the best formula involving only W and H will be the one which gives a certain best relative importance to W and H.

Both of the above formulas were carefully investigated by applying them to the nine subjects that had been measured in the laboratory. For these subjects W, H[4] and A are known. In testing a formula the procedure was to solve for C (the only unknown) for each of the ten cases and then to assume the correct constant for the formula to be the average value of the C's so found. The merit of the

4. With about half the subjects this was determined standing. No attempt has been made to correct for the difference between height and length. (See Footnote 3, p. 10. The largest difference we have found would cause a change of about 1.5 per cent. in the surface area and reading. This is within the limit of accuracy claimed for the Height-Weight Chart.

formula was then judged by the percentage variation of the factors C, as found for the individual cases, from the constant chosen. This percentage variation would also be the percentage error in area in the individual cases if the formula were applied using the chosen constant.

The formulas with H^1 and $H^{1/2}$ both gave rather good results, but it was noticed in a number of cases that the percentage error for the same subject differed in sign for the two formulas. This would indicate that some formula would be better than either of these two if H were raised to some power between ½ and 1.

The formula $A = W^{1/3} \times H \times C$ can also be written $A = W^{1/3} \times H^{1/1} \times C$, bringing it into the same form as $A = W^{1/2} \times H^{1/2} \times C$ and the general form of this formula can be written $A = W^{1/a} \times H^{1/b} \times C$. In order that the expression $W^{1/a} \times H^{1/b} \times C$ may remain bidimensional it is only necessary that $3/a \times 1/b = 2$, as it does in the two cases considered. For an intermediate equation it is obvious that (b) must be greater than 1 but less than 2. A value of $b = 1.25$ would give $a = 2.5$ and the formula would be $A = W^{1/2.5} \times H^{1/1.25} \times C$. This formula when tested gave very much better results than either of the others, but to find the best values of "a" and "b" it was necessary to explore formulas having a number of other combinations of "a" and "b" and then to interpolate graphically.

The best values of "a" and "b" were found to be $a = 2.35$ and $b = 1.38$ giving the formula the final form of $A = {}^{1/2.35} \times H^{1/1.38} \times C$ or $A = W^{0.425} \times H^{0.725} \times 71.84$. This formula can be solved by logarithms as follows:

$$\text{Log. } A = \text{Log. } W \times 0.425 + \text{Log. } H \times 0.725 + 1.8564.$$

1.8564 is a constant equal to Log. C.

In order to make this somewhat complicated formula easy of application a chart has been constructed (Fig. 2). By means of this it is possible to find the approximate surface area at a glance. The ordinates represent the height in centimeters, the abscissae the weight in kilograms. The point of intersection of these lines is found for any given subject and the surface area in square meters read off on the curved lines by interpolation. The second decimal place, which is never accurate, is estimated by the distance of the point from the nearest curved line. For instance, if the man were 150 centimeters tall and weighed 60 kilograms, the approximate surface area would be 1.55 square meters.

The large plus error in the constant employed by Meeh[5] has been established by the previously quoted works of Bouchard, Lissauer, Sicheff, Lassabliere and ourselves. According to our calculations the

5. Meeh: Ztschr. f. Biol., 1879, xv, 425.

average error in Meeh's constant is about 15 per cent. Instead of a uniform figure of 12.312, the "constant" should average about 10.5, varying between 12.3 for the greatly emaciated and 9.0 for the very stout. We must remember that figures for the calories per square meters of body surface will average 15 per cent. smaller when Meeh's formula is used then when the linear formula or the new Height Weight Formula" is employed.

SUMMARY AND CONCLUSIONS

The method of calculating the surface area from the so-called "Linear Formula" is given with a slight correction in the factor for the arms and an alternative measurement for the thighs. A simpler "Height-Weight Formula" has been devised to estimate the surface of subjects if only their height and weight be known. This is expressed in the terms $A = W^{0.425} \times H^{0.725} \times C$. A being the surface area in square centimeters, H the height in centimeters, W the weight in kilograms and C the constant, 71.84. A chart has been plotted from this formula so that the approximate surface area may be determined at a glance.

We may estimate the errors in the various formulas as follows: "Linear Formula" and "Height-Weight Formula," maximum $\pm$ 5 per cent., average $\pm$ 1.5 per cent., Meeh's Formula, maximum $+$ 30 per cent., average $+$ 15 per cent. In general the maximum figures apply only to those of unusual shape, while with those of average body form the average error will seldom be exceeded.

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CLINICAL CALORIMETRY

ELEVENTH PAPER

A COMPARISON OF THE METABOLISM OF MEN FLAT IN BED AND SITTING IN A STEAMER CHAIR *

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This paper and those which follow it are based on results obtained with the Sage calorimeter, which was described a year ago in the first two papers of the series. At that time the policy was adopted of publishing all the alcohol checks to show the accuracy of the apparatus throughout the year. It gives considerable satisfaction to report that the uniformly good results previously obtained have been repeated in this, the third season in which the calorimeter has been used. After a period of several weeks needed to put the apparatus in order, a good check was made Oct. 22, 1914, and not till then were the experiments begun. Although there was no reason to suspect trouble with the apparatus, tests were made Nov. 28, 1914, Jan. 1, 1915 and also on May 19, 1915, after the last experiment for the season was completed. The results are recorded in Table 1 in which it will be seen that the total errors were as follows: heat, + 0.51 per cent., oxygen — 0.51 per cent., carbon dioxid — 0.36 per cent., water + 3.13 per cent. The respiratory quotient averaged 0.666, while the theoretical quotient is 0.6667.

Since the publication of Paper 2[1] a new valve has been designed by one of the authors (G. F. S.) and has been attached to the absorber table, with most satisfactory results. The three-way valves by means of which the air current was switched from one set of absorbing bottles to the other required constant attention to prevent leaks. The new valves have been used in about ninety experiments and have required repairs but once. The details are shown in Figure 1.

The calorimeter bed has been the subject of much experimentation. The oak frame on skids has proved satisfactory from the start, but the springs under the subjects sagged too much and the blanket covering

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1. Riche and Soderstrom: Chemical Calorimetry, Paper 2, The Archives Int. Med., 1915, xv, 805.

the springs stored too much heat. A waterproof canvas, substituted for the springs, was more comfortable, but heat was accumulated underneath the subject and was suddenly liberated whenever he moved. This made the heat control difficult. During the last year a comfortable hammock made of fish net has given excellent results. Comparatively little heat is banked up underneath the man and when he turns over the liberation of heat is only one half or three quarters as great as in previous years to judge from the expansion of air in the box. This means that a given reading on the work-adder in the season of 1914-1915 indicates a little more activity on the part of the subject than the same reading in previous years.

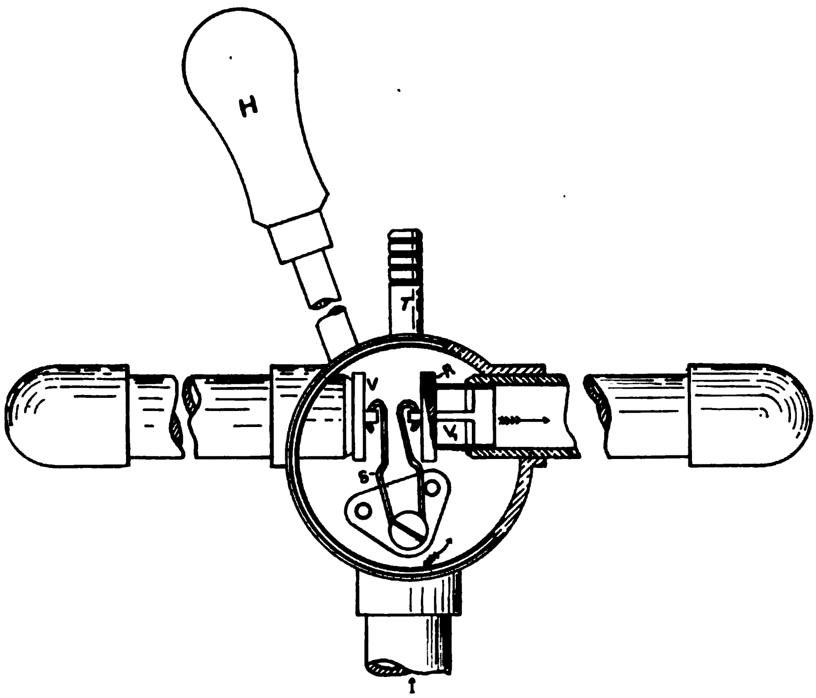

Fig. 1.—Double throw valve for absorber table: H, handle; T, tube through which sample of air can be removed; S, piano wire spring to open and close valves V and V_1; R, rubber washer acting as seat for valve.

Figure 2 shows the bed with the oak frame and hammock. Figure 3 shows the steamer chair used after Jan. 8, 1915. It is very comfortable for the average subject, and even some of those who were not orthopneic preferred it to the bed.

In recording the movements of the spirometer at the close of each hour we have used a pen (Fig. 4) which enables us to dispense with smoked paper. A glass tube a little more than 2.5 cm. long and 9 mm. in diameter is sealed at one end. The other end is closed by means of

cork and sealing wax, through which passes a fine capillary tube bent at a right angle. The capillary passes nearly to the bottom of the tube. The tube is filled with ink, containing a little glycerin. This simple apparatus seems to work even better than the expensive article of commerce which has a platinum tube.

When the calorimeter was planned it was built high enough at one end to allow a man to sit upright. This was essential if orthopneic, cardiac or nephritic patients were to be studied. It soon became evident

Fig. 2.—New calorimeter bed.

that normal subjects should be studied while lying flat and also while sitting with a back rest to serve as controls. The form and accuracy of the Sage calorimeter seemed to lend itself particularly well to this investigation, which requires a greater delicacy of technic than has previously been available.

Fig. 3.—Steamer chair for calorimeter.

Katzenstein[2] in 1891 found that the metabolism of his subjects was higher when standing than when lying and that the increase was comparatively slight if the man were standing in a comfortable relaxed position. Winternitz and Pospischil[3] found the carbon dioxid output

2. Katzenstein, G.: Ueber die Einwirkung der Muskeltätigkeit auf den Stoffwechsel der Menschen, Arch. f. d. ges. Physiol., 1891, xlix, 330.

3. Winternitz and Pospischil: Ueber den respiratorischen Stoffwechsel unter thermischen und Mechanischen Einflussen, Bl. f. klin. Hydrotherapie, 1893, 3, 7, 30, 49, 62.

lowest while lying, higher while sitting and still higher while standing. Some of their quotients are so low as to suggest doubts as to the technic. Johansson[4] determined the carbon dioxid production with scrupulous care to avoid the disturbing influences of muscular movement. He found that the output was about 6 per cent. higher while sitting than while lying, but he gives no details as to the exact postures used. Widlund[5] found no apparent rise in metabolism when the man stood if the muscular relaxation were complete. Benedict and Carpenter[6] have compared the metabolism of their subjects in two different calorimeters. Their bed calorimeter is smaller than the Sage instrument and the subjects lie flat during the experiments, are very quiet and often go to sleep. Their chair calorimeter contains a comfortable armchair, tilted slightly backwards but without a head rest. In this chamber the subjects are not absolutely quiet, but are allowed to read. The

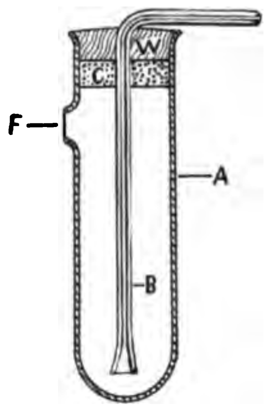

Fig. 4.—Capillary writing pen: A, glass reservoir for ink; F, opening for filling; C, cork; W, sealing-wax; B, capillary glass tube.

matter is critically treated by Benedict and Joslin,[7] who conclude that the increase in metabolism of a subject while sitting in a chair and awake over that when lying asleep varies from 20 to 30 per cent. The question was further studied by Emmes and Riche[8] in the same labora-

4. Johansson, J. E.: Ueber den Tageschwankungen des Stoffwechsels und der Körpertemperatur im nüchternen Zustand und vollstandlichen Muskelruhe, Skand. Arch. f. Physiol., 1898, viii, 85.

5. Widlund, K. E.: Untersuchung des Verhaltnisses zwischen CO_2 Produktion in Rühelage und im stehenden Stellung, Skand. Arch f. Physiol, 1905, xvii, 290.

6. Benedict and Carpenter: Metabolism and Energy Transformation of Healthy Man During Rest, Carnegie Institution of Washington, Pub. 126, 1911, p. 242.

7. Benedict and Joslin: Metabolism in Diabetes Mellitus, Carnegie Institution of Washington, Pub. 136, 1910, p. 175.

8. Emmes, L. E., and Riche, J. A.: The Respiratory Exchange as Affected by Body Position, Am. Jour. Physiol., 1911, xxvii, 406.

tory, using the Benedict Universal Respiration Apparatus to which the subjects were attached by means of nose pieces. They found the oxygen consumption averaged 7.6 per cent. higher when they were sitting upright in a chair with the head supported than when lying flat. This they considered due primarily to the difference in the internal muscular activity necessitated by the sustaining of body parts. They call attention to the fact that the pulse rate is 5 to 10 per cent. higher when sitting. Higgins,[9] also of the Nutrition Laboratory, studied the effect of posture on the tension of carbon dioxid in the alveoli, and found it highest with the subject lying on his back or side, lower in the Trendelenburg and semireclining position, still lower while sitting erect and lowest while standing.

DESCRIPTION OF SUBJECTS OF EXPERIMENTS

John L., 44 years old, 174.7 cm. tall, normal control, history given in Paper 4.[10] March 26, 1914, he lay flat on the canvas bed. April 3 he sat propped up in bed at an angle of about 50 degrees, leaning against a firm back rest, padded with pillows, which supported his head.

Albert G., 24 years old, 162.2 cm. tall, normal control. He is a laborer, born in Italy. He remembers no illnesses except a slight skin eruption fourteen years ago. His health is good but he has been out of work for some time. He is short, stocky, fairly muscular, with little fat. Heart and lungs normal. Admitted to the metabolism ward Dec. 14, 1914, discharged Jan. 14, 1915. From January 4 to 14 he had a very mild sore throat, with slight afternoon fever. January 13 at 10 a. m., he was given subcutaneously a dose of New York City Board of Health typhoid vaccine consisting of one-half billion dead bacilli. There was a slight normal reaction with moderate swelling at the site of injection.

The young Italian was rather neurotic, and after a couple of weeks of enforced idleness in the ward began to develop imaginary pains. He left the hospital in high dudgeon, but when his wages were spent in the course of the next two weeks he returned asking for his job as normal control.

December 21, lying flat in bed, he was unusually quiet, sleeping twenty-four minutes in the first hour and about six minutes in the second. Two days later, propped up at an angle of about 45 degrees with the back rest, he was not so quiet. The third period had to be discarded from the calculations because he slid down in the bed until the body was at about half its original angle. December 28 he was in the calorimeter for two periods, each one and one-half hours long. He was lying flat and very quiet, dozing most of the time. December 30 an experiment was made after the ingestion of 79 gm. of olive oil. January 4 and 6 tests were made after 115 gm. commercial glucose. On the eighth a three hour basal determination was made. He slept fifty-five minutes in the first hour and was somewhat restless in the other hours. The next day he was in the calorimeter, sitting in the steamer chair which had just been finished. In the first hour he was somewhat restless, in the second hour quiet. Unfortunately the urine specimen was lost on this day.

R. H. S., man, 21½ years old, chemist, normal control. Except for measles, scarlet fever and a broken arm in childhood he has never been sick in bed. He

9. Higgins, H. L.: The Influence of Food, Posture and Other Factors on the Alveolar Carbon Dioxid Tension in Man, Am. Jour. Physiol., 1914, xxxiv, 114.

10. Gephart and DuBois: Clinical Calorimetry, Paper 4, The Archives Int. Med., 1915, xv, 835.

TABLE 1.—ALCOHOL CHECKS

Date	Hour	Heat				Oxygen			Carbon Dioxid			Water			R. Q. Theory, (0.667)
		Alcohol Burned, Gm.*	Theory, Cal.	Found, Cal.	Error, %	Theory, Gm.	Found, Gm.	Error, %	Theory, Gm.	Found, Gm.	Error, %	Theory, Gm.	Found, Gm.	Error, %	
10/22/14	1	12.22	78.14	77.14	—1.2	23.02	22.56	—1.9	29.01	20.92	—0.8	13.82	15.82	+10.8	0.672
	2	11.96	76.48	75.19	—1.6	22.52	22.77	+1.1	20.64	20.41	—1.1	13.84	14.64	+5.7	0.652
	3	11.93	76.29	75.47	—1.0	22.47	21.85	—2.7	20.59	20.25	—1.6	13.81	14.33	+3.7	0.674
Average........	...	.....	76.97	75.98	—1.3	22.69	22.39	—1.3	20.77	20.53	—1.1	13.82	14.76	+6.8	0.666
11/27/14	1	11.96	76.49	77.74	+1.6	22.52	22.17	—1.5	20.64	20.55	—0.4	13.84	14.14	+2.1	0.674
	2	12.23	78.21	78.36	+0.2	23.08	23.04	±0.0	21.11	21.06	—0.2	14.15	14.19	+0.2	0.664
	3	12.56	80.32	80.84	+0.6	23.65	23.40	—1.0	21.68	21.47	—0.9	14.53	14.60	+0.4	0.667
Average........	...	.....	78.34	78.98	+0.8	23.07	22.87	—0.8	21.14	21.03	—0.5	14.17	14.31	+1.0	0.668
1/18/15	1	13.67	87.41	89.35	+2.2	25.74	25.89	+0.9	23.60	23.19	—1.7	15.82	16.34	+3.2	0.652
	2	13.54	86.58	88.99	+2.7	25.50	25.81	+1.2	23.37	23.54	+0.7	15.67	16.27	+3.8	0.663
	3	13.62	87.09	87.17	+0.06	25.65	24.99	—2.5	23.51	23.13	—1.6	15.76	15.82	+0.3	0.673
Average........	...	.....	87.03	88.50	+0.5	25.63	25.56	—0.2	23.49	23.29	—0.8	15.75	16.14	+2.4	0.663
5/19/15	1	10.46	66.89	67.23	+0.5	19.70	19.85	+0.7	18.05	18.19	+0.7	12.10	12.52	+3.4	0.666
	2	10.41	66.57	66.21	—0.5	19.60	19.35	—1.27	17.97	17.75	—1.2	12.04	12.29	+2.0	0.667
	3	10.20	65.23	66.72	+2.2	19.21	19.54	+1.72	17.21	18.08	+5.0	11.80	12.12	+2.7	0.673
Average........	...	.....	66.23	66.72	+0.7	19.50	19.58	+0.4	17.74	18.01	+1.5	11.98	12.31	+2.7	0.669
Total......	...	.....	925.69	930.41	+0.51	272.61	271.22	—0.51	249.46	248.54	—0.36	167.18	172.58	+3.13	Av. 0.666+

* In most of the tests the solution contained 90.32% by weight of ethyl alcohol.

TABLE 2.—Data of—

Subject, Date, Weight, Surface Area Linear Formula	Period	End of Period Time	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N. per Hour, Gm.	Indirect Calo-rimetry, Cal.	Heat Elimi-nated, Cal.
John L. .... 3/26/14 70.94 Kg.	Prelim.	11:20	.....	.....	....	.....	.....	......	.....
	1	12:20	21.12	19.51	0.79	25.77	0.363	64.65	66.00
	2	1:20	21.37	19.62	0.79	24.56	0.363	65.10	68.26
	3	2:20	21.07	19.97	0.78	24.01	0.363	65.85	66.72
								195.20	
John L. .... 4/3/14 70.90 Kg.	Prelim.	12:05	.....	.....	....	.....	.....	......	.....
	1	1.05	20.36	18.33	0.81	22.90	0.347	61.08	61.79
	2	2:05	19.94	18.47	0.79	23.66	0.347	61.19	63.45
								122.27	
Albert G. .... 12/21/14 66.03 Kg. 1.67 Sq. M.	Prelim.	11:13	.....	.....	....	.....	.....	......	.....
	1	12:13	24.32	20.68	0.86	31.28	0.60	69.31	75.78
	2	1:13	25.97	20.96	0.90	31.59	0.60	71.08	78.38
	3	2:13	24.31	21.22	0.83	31.86	0.60	70.73	78.17
								211.12	
Albert G. .... 12/23/14 63.08 Kg. 1.63 Sq. M.	Prelim.	11:09	.....	.....	....	.....	.....	......	.....
	1	12:09	24.73	20.43	0.88	23.81	0.636	68.89	62.75
	2	1:09	23.44	20.22	0.84	26.68	0.636	67.53	68.59
	3	2:09	26.11	23.15	0.82	28.22	0.636	77.07	69.69
								213.49	
Albert G. .... 12/28/14 65.35 Kg. 1.66 Sq. M.	Prelim.	11:05	.....	.....	....	.....	.....	......	.....
	1	12:35	34.28	28.96	0.86	39.12	0.731	97.54	112.08
	2	1:05	35.30	29.23	0.89	39.24	0.731	99.06	107.08
								196.60	
Albert G. .... 1/8/15 66.33 Kg. 1.67 Sq. M.	Prelim.	11:21	.....	.....	....	.....	.....	......	.....
	1	12:21	22.43	19.88	0.82	27.86	0.661*	66.09	68.19
	2	1:21	25.06	20.38	0.89	29.56	0.518*	69.16	72.48
	3	2:21	24.92	22.81	0.79	30.70	0.518	75.51	71.82
								210.76	
Albert G. .... 1/9/15 65.85 Kg. 1.67 Sq. M.	Prelim.	11:13	.....	.....	....	.....	.....	......	.....
	1	12:13	25.85	21.50	0.86	33.84	.....	72.89	75.78
				19.07	0.90	32.76	.....	65.32	76.38
	2	1:13	23.62						
								138.21	
				.....	....	.....	.....	......	.....
R. H. S. .... 4/19/15 64.36 Kg. 1.88 Sq. M.	Prelim.	11:40	.....						
				19.95	0.85	26.28	0.478	66.98	79.97
	1	12:40	23.21						
				20.87	0.83	26.25	0.478	69.82	77.61
	2	1:40	23.79						
								136.80	

* Calculations for first period were based on a mean of these two figures.

—Calorimeter Experiments

Direct Calorimetry (Rectal Temp.), Cal.	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M. (Meeh)	
.....	37.11	..	....	....	..	..	..	....	.....	Basal
52.70	36.89	61	18.0	0.78	15	62	23	0.90	30.64	Flat in bed
68.56	36.94	55	18.0	0.79	15	61	24	0.90	30.85	
62.04	36.88	57	33.7	0.76	15	69	16	0.90	31.21	
183.30										
.....	36.89	..	....	....	..	..	..	....	.....	Propped up with back rest
57.31	36.82	59	23.0	0.81	15	55	30	0.86	28.96	
60.47	36.80	62	27.0	0.78	15	63	22	0.86	29.01	
117.78										
.....	37.11	..	....	....	..	..	..	....	.....	Basal, flat in bed
69.44	37.00	58	12.5	0.87	23	34	43	1.05	34.45	Asleep 24 min.
72.03	36.89	54	14.6	0.93	22	19	59	1.08	35.33	Asleep 6 min.
73.58	36.85	52	14.7	0.84	22	42	35	1.07	35.15	
215.05										
.....	37.13	..	....	....	..	..	..	....	.....	Propped up at angle of 45 deg.
58.62	36.96	54	17.1	0.91	25	23	52	1.10	35.33	Quiet
68.25	36.96	54	14.6	0.86	25	36	39	1.07	34.63	Quiet
71.24	37.01	56	19.0	0.88	22	45	33	1.22	39.52	Slid down in bed
198.11										
.....	36.79	..	....	....	..	..	..	....	.....	Basal. Flat
116.76	36.85	52	12.2	0.88	20	33	48	1.00	32.55	Dozed
96.84	36.69	58	19.0	0.91	20	25	56	1.01	33.05	Dozed. Periods 1½ Hrs. long
213.60										
.....	36.74	..	....	....	..	..	..	....	.....	Basal, flat in bed
65.19	36.68	58	8.5	0.88	24	44	32	1.00	32.77	Asleep 55 min.
70.68	36.62	56	29.0	0.92	20	22	58	1.07	35.09	Restless
73.59	36.68	55	27.2	0.79	18	58	23	1.14	37.44	Restless
209.46										
.....	37.06	..	....	....	..	..	..	....	.....	In steamer chair
66.58	36.90	62	18.0	....	..	..	..	1.11	36.30	Restless
73.98	36.84	59	14.0	....	..	..	..	0.99	32.55	Quiet Urine spec. lost
140.56										
.....	37.12	..	....	....	..	..	..	....	.....	Basal, flat in bed
72.65	36.99	60	1.0	0.86	19	39	243	1.04	33.88	Almost motionless
71.40	36.89	60	6.0	0.84	18	45	37	1.09	35.32	Almost motionless
144.05										

TABLE 2.—

Subject, Date, Weight, Surface Area Linear Formula	Period	End of Period Time	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	per Hour, Urine N. Gm.	Calo-rimetry, Indirect Cal.	Elimi-nated, Heat Cal.
R. H. S.	Prelim.	11:22	.....	.....	....	.....	.....	......	.....
4/21/15 63.35 Kg.	1	12:22	21.55	18.69	0.84	24.82	0.398	65.76	76.49
1.78 Sq. M.	2	1:22	21.94	18.84	0.85	25.37	0.398	58.54	76.96
								124.30	
E. F. D. B.	Prelim.	11:17	.....	.....	....	.....	.....	......	.....
5/6/15 74.64 Kg.	1	12:17	23.48	21.39	0.80	31.59	0.528	70.75	70.84
1.91 Sq. M.	2	1:17	23.69	22.04	0.78	32.82	0.528	72.78	73.96
								143.53	
E. F. D. B.	Prelim.	11:18	.....	.....	....	.....	.....	......	.....
5/7/15 74.20 Kg.	1	12:18	23.12	20.51	0.82	33.52	0.593	68.22	76.92
1.90 Sq. M.	2	1:18	23.45	20.73	0.82	31.68	0.593	68.96	75.07
								137.18	
William A.	Prelim.	11:13	.....	.....	....	.....	.....	......	.....
1/25/15 63.44 Kg.	1	12:13	25.32	20.31	0.91	34.45	0.382	69.44	72.58
1.80 Sq. M.	2	1:13	24.08	20.86	0.84	32.15	0.382	70.14	73.06
	3	2:13	24.45	22.02	0.81	31.11	0.382	73.44	73.48
								213.02	
William A.	Prelim.	10:40	.....	.....	....	.....	.....	......	.....
1/27/15 63.00 Kg.	1	11:40	24.37	21.08	0.84	32.50	0.390	70.86	73.83
1.74 Sq. M.	2	12:40	25.01	22.17	0.82	32.37	0.390	74.09	75.33
	3	1:40	24.75	23.05	0.78	33.58	0.390	76.38	78.06
								221.33	
Theodore S.	Prelim.	11:10	.....	.....	....	.....	.....	......	.....
1/28/14 59.52 Kg.	1	12:10	23.13	20.30	0.83	39.08	0.454	67.86	77.23
	2	1:10	23.98	21.43	0.81	38.26	0.454	71.40	76.66
Theodore S.	Prelim.	11:15	.....	.....	....	.....	.....	......	.....
1/30/14 59.44 Kg.	1	12:15	21.66	18.76	0.84	36.00	0.385	62.97	78.11
	2	1:15	22.80	20.18	0.82	37.75	0.385	67.48	78.83
Theodore S.	Prelim.	11:46	.....	.....	....	.....	.....	......	.....
2/5/14 60.28 Kg.	1	1:16	34.68	31.59	0.80	50.61	0.538	105.10	118.65
	2	2:16	22.82	20.58	0.81	32.00	0.538	68.47	72.40
Theodore S.	Prelim.	11:50	.....	.....	....	.....	.....	......	.....
2/9/14 61.15 Kg.	1	12:50	21.11	18.41	0.83	21.14	0.394	61.66	56.98
	2	1:50	22.34	19.11	0.85	22.55	0.394	64.30	60.88
Theodore S.	Prelim.	11:10	.....	.....	....	.....	.....	......	.....
2/13/14 61.99 Kg.	1	12:10	24.54	20.49	0.87	26.73	0.391	69.38	70.40
	2	1:10	24.35	21.15	0.84	33.09	0.391	71.02	75.79

—(*Continued*)

Direct Calorimetry (Rectal Temp.), Cal.	Rectal Temp., C.	Average Pulse	Work Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M. (Meeh)	
.....	37.00	..	....	..:.	..	..	..	....	.....	In steamer chair
67.20	36.83	62	1.0	0.83	16	49	36	1.04	33.60	Almost motionless
78.30	36.86	57	6.0	0.86	18	39	43	0.92	29.91	Almost motionless
145.50										
.....	36.99	..	....	....	..	..	..	....	.....	Basal, flat in bed
69.89	36.98	57	10.0	0.79	20	57	23	0.95	32.40	Very quiet
75.52	37.01	57	7.0	0.78	19	68	13	0.98	33.82	Very quiet
145.41										
.....	36.92	..	....	....	..	..	..	....	.....	In steamer chair
67.38	36.76	57	9.0	0.83	23	45	33	0.92	32.12	Quiet
78.32	36.83	55	12.0	0.83	23	45	33	0.93	32.47	Quiet
145.70										
.....	36.96	..	....	....	..	..	..	....	.....	Cardiac patient; flat in bed
62.29	36.77	62	20.0	0.93	15	20	65	1.10	35.47	Restless
69.48	36.71	60	11.0	0.85	14	68	18	1.10	35.82	Fairly quiet
70.55	36.66	62	10.0	0.81	14	62	24	1.16	37.51	Quiet
202.32										
.....	.....	..	....	....	..	..	..	....	.....	In steamer chair
66.72	36.76	66	10.0	0.85	15	44	42	1.18	36.36	Quiet
72.33	36.71	66	11.0	0.82	14	53	33	1.18	38.01	Quiet
73.06	36.62	..	21.0	0.78	14	65	22	1.21	39.19	Fairly quiet
212.11										
.....	37.14	..	....	....	..	..	..	....	.....	Cardiac patient; flat on back
89.92	36.94	49	21.0	0.84	18	46	36	1.14	36.14	Restless
71.30	36.93	50	28.0	0.82	17	52	31	1.20	38.08	Restless
.....	37.10	..	....	....	..	..	..	....	.....	Propped up in bed at angle of about 30 deg.
70.46	37.05	53	1.9	0.85	16	44	40	1.06	33.58	
75.61	37.13	52	0.9	0.83	15	51	34	1.14	35.99	
.....	37.03	..	....	....	..	..	..	....	.....	Flat on back; quiet both periods. Pain in hand at 12:43. Periods 1½ Hrs.
86.70	36.87	50	10.0	0.80	14	60	26	1.16	37.09	
72.40	36.94	47	0.6	0.81	14	56	30	1.14	36.26	
.....	37.06	..	....	....	..	..	..	....	.....	Propped up in bed at angle of 50 deg. Quiet both periods
64.71	36.83	49	6.7	0.84	17	45	38	1.01	32.28	
67.15	36.86	46	3.7	0.86	16	40	44	1.05	33.67	
.....	37.01	..	....	....	..	..	..	....	.....	Flat on back
66.94	36.95	54	3.5	0.88	15	34	51	1.12	35.99	Quiet
75.32	36.95	55	5.5	0.84	15	45	40	1.15	36.84	Quiet

is accustomed to take moderate exercise and his general health is fair. This last year he has been doing much night work, has taken no exercise, and has lost about 5 pounds in weight. He is very tall, 184.2 cm. and very thin, but not emaciated. His measurements and surface area are given in detail in Paper 9 of this series. His heart and lungs, etc., are normal.

April 19, 1915, he was in the calorimeter flat in bed for two hours to determine the basal metabolism, and two days later was in the steamer chair for a similar period. On both days he was awake but almost motionless.

E. F. D. B., man, 33 years old, a normal control, whose history is given in Paper 4[19] of this series. May 6, 1915, he was in the calorimeter flat in bed. Except for a small cup of black coffee without sugar, he had taken no food since 7:30 p. m. The steamer chair experiment, owing to a sudden change in plans, had to be made the next day. Unfortunately the subject had eaten a Welsh rarebit at 11 p. m., so it is possible that there was a slight specific dynamic action increasing the metabolism. He was quiet in both experiments.

CARDIAC PATIENTS

Theodore S., 32 years old, coachman, born in Sweden. Admitted Jan. 17, 1914, discharged February 22. Diagnosis, mitral stenosis, cardiac hypertrophy and dilatation, auricular fibrillation.

History.—Pneumonia when 6 years old, no rheumatism. Four or five years prior to admission the patient began to have shortness of breath on exertion. Three years previous to admission this compelled him to look for an easy job, but he was able to carry trunks upstairs until eight months prior to admission. For the previous two weeks the dyspnea had confined him to bed.

Physical Examination.—Of medium build, 169 cm. tall, well nourished and fairly muscular. He is slightly dyspneic, the lips are a deep red color, with a slight purplish tint. He has an occasional cough. The apex is in the fifth costal interspace 12 cm. from the midline, the left limit of dulness 14.5 cm. from midline, the right limit in the fourth space 4 cm. from midsternum. The action is slow and very irregular in force and frequency. Phlebograms show auricular fibrillation. At the apex is heard the presystolic murmur to which Mackenzie and Lewis have recently called attention. The first sound is sharp and short, the second sound faint, followed immediately by a loud, rough, rumbling murmur which diminishes during diastole, lasting through the short diastoles but followed by a period of silence in the long pauses. The pulse is small, the arteries palpable. There are a few subcrepitant râles at the bases of the lungs. The Wassermann reaction is negative. By January 26 all dyspnea had disappeared and there was not the slightest trace of orthopnea. He was able to sit in a chair without fatigue. There was no edema.

Experiments.—January 28, basal experiment flat in bed. The patient was anxious to cooperate but he was of timid nature and during this first observation was a little anxious. His skin was cold and clammy at the start and he sweated profusely while in the calorimeter. January 30 he was propped up on the calorimeter bed at an angle of about 30 degrees. He was quieter than before. February 5 he was in the calorimeter flat in bed. Just as the first period was being ended he had a slight pain in his hand which caused him to sweat. This suddenly expanded the air in the box and raised the work adder 5 cm. The first period was prolonged one-half hour, by which time things had come into equilibrium. February 9 he was propped up with the back rest at an angle of about 50 degrees and made very comfortable with pillows at his back and under his knees. February 13 a third experiment with the patient flat in bed was made. He was comfortable and quiet but apparently began to sweat a little when signalled to lie quiet at the end of each period.

February 16 the systolic blood pressure was 145 mm. lying down and 142 mm. when sitting up at an angle of about 45 degrees. February 22 he was discharged in good condition and was able to walk up two flights of stairs slowly

without dyspnea. March 4 he was readmitted with a sharp attack of bronchopneumonia from which he recovered, leaving the hospital on the 27th of that month.

William A., 24 years old, laborer. Admitted to the hospital Dec. 28, 1914, discharged Jan. 30, 1915. Diagnosis, aortic insufficiency, cardiac hypertrophy and dilatation. History. Has had measles, pneumonia, rheumatism and urethritis and has had frequent attacks of tonsillitis. December 25 he had a sudden sharp pain in the side. The following night he was very orthopneic and had a great deal of palpitation. He complains also of weakness and cough.

TABLE 3.—Summary of Calorimeter Experiments on Body Posture

Subjects	Age, Years	Weight, Kg.	Average Pulse	R. Q.	Average Calories per Hour		Posture
					Indirect Calorimetry	Direct Calorimetry	
Normals							
John L.	44						
3/26/14	..	70.94	58	0.78	65.20	61.10	Lying*
4/ 8/14	..	70.90	61	0.80	61.14	58.89	Sitting up
Albert G.	24						
12/21/14	..	66.08	54	0.86	70.37	71.68	Lying
12/23/14	..	68.08	54	0.85	71.16	64.37	Sitting up
12/28/14	..	65.35	53	0.88	96.30	106.80	Lying
1/ 8/15	..	66.33	56	0.84	70.25	69.82	Lying
1/ 9/15	..	65.85	61	0.88	69.10	70.28	Sitting up
R. H. S.	21						
4/19/15	..	64.36	60	0.84	68.40	72.08	Lying
4/21/15	..	63.85	59	0.84	62.15	72.75	Sitting up
E. F. D. B. ..	33						
5/ 6/15	..	74.64	57	0.79	71.77	72.71	Lying
5/ 7/15	..	74.20	56	0.82	68.59	72.85	Sitting up
Cardiacs							
William A. ..	24						
1/21/15	..	63.44	61	0.85	71.01	67.44	Lying
1/27/15	..	63.00	66	0.81	73.78	70.70	Sitting up
Theodore S.	32						
1/28/14	..	59.52	50	0.82	69.63	80.26	Lying
1/30/14	..	59.44	53	0.83	65.23	73.04	Sitting up
2/ 5/14	..	60.28	49	0.80	86.79	76.01	Lying
2/ 9/14	..	61.15	48	0.84	62.98	65.93	Sitting up
2/13/14	..	61.99	55	0.85	70.20	71.13	Lying

* Basal—flat in bed.

Physical Examination.—Tall (180 cm.), well developed and well nourished; dyspneic and orthopneic; color pale.

Tonsils swollen and congested. Apex impulse diffuse, left border 13 cm. right border 4 cm. from midline. There is a waterfall diminuendo diastolic murmur and a presystolic roughness considered to be a Flint murmur. The pulse is Corrigan in type.

The temperature, which has been slightly elevated, dropped to normal and the dyspnea and orthopnea disappeared. A blowing systolic murmur became

audible in the aortic region. By January 26 he was able to sit all day in a chair without fatigue.

January 25 he was in the calorimeter flat on his back for three hours, and two days later was in the steamer chair for a similar period.

METHODS OF EXPERIMENTS

The calorimeter and the experimental procedure have been described in Papers 1 to 4 of this series. All the experiments were made in the morning without food, except in a few instances when a small cup of black coffee without sugar was used. When the subjects were flat in bed they were allowed a pillow under the head, and if they desired it, one under the knees.

DISCUSSION OF RESULTS

Each experiment in the sitting posture is controlled by one or more observations on the same individual lying flat in bed, and we might therefore compare the average calories per hour produced under the

TABLE 4.—SUMMARY OF RESULTS

Name	Average Pulse		Average Metabolism, Cal. per Sq. M. per Hour, Meeh		Per Cent. Difference in Semireclining
	Lying	Semireclining	Lying	Semireclining	
Normal Controls					
John L.	58	61	30.90	28.99	—6.1
Albert G.	54	58	*34.29	34.71	+1.2*
R. H. S.	60	59	34.60	31.75	—8.2
E. F. D. B.	57	56	32.86	32.29	—1.7
Cardiac Cases					
Theodore S.	51	51	36.73	33.89	—7.7
William A.	61	66	36.27	37.85	+4,4
Average.........	..	..	.....	.....	—3.0

* Omitting experiment of December 28, averages are: metabolism, lying equals 35.04; per cent. difference equals —1.0.

two conditions. The standard procedure in this laboratory, however, has been to compare the results in terms of calories per square meter of surface area per hour. This latter method will be adhered to, since these experiments will be discussed from other points of view in the following papers. It makes little difference which method is used, as the surface area scarcely changed at all between experiments.

The results are summarized in Tables 3 and 4. It will be seen that the metabolism averaged 3 per cent. lower in the semireclining than in the lying posture. Of the four normal subjects, three showed this lower metabolism very clearly. In one, Albert G., the average figure for the flat experiments is 1.2 per cent. lower, but if the abnormally low result in the experiment of December 28, when he dozed, be

excluded, the balance will be 1.0 per cent. on the other side of the line. It is unfortunate that it was not possible to have more cardiac patients in the series. The mitral case repeatedly showed a lower metabolism when propped up in bed; the aortic patient showed the opposite. Taken as a whole, the differences are so small that we may use the same figure for the average normal metabolism in both postures, and we need hardly change our normal base line when we discuss the experiments on patients who were so orthopneic that they had to use the steamer chair while in the calorimeter.

These results were somewhat surprising as the general opinion in the laboratory was that the heat production would be 5 to 10 per cent. higher in the steamer chair. It must be remembered that previous investigators have used chairs in which the subjects sat upright or nearly upright, in some cases the head being unsupported. All the experimenters agreed that there was some muscular effort needed to maintain the posture and they ascribed to this the increase in heat production. In the orthopneic posture either with back rest or steamer chair as used in these calorimeter experiments, there was complete support of the body and head. No more muscular tension was needed than when the subjects were lying flat and the pillows were so arranged that the men could fall asleep without change in posture. It is quite possible that the diminished pressure on the diaphragm lessened the work of breathing enough to account for the lower metabolism.

On steamers, in clubs, and in those parts of our country where laziness is a science, men assume a semireclining posture with the head, back and feet supported on any convenient object. Patients who are very dyspneic are obliged to sit up and they can sleep only in the semireclining posture. The slight diminution in energy requirement may be a factor in leading them to assume the orthopneic posture, but with many cardiac and nephritic patients this economy is more than offset by increased muscular activity.

SUMMARY AND CONCLUSIONS

The Sage calorimeter in the season of 1914-1915 was fully as accurate as in the previous years. Alcohol checks gave the following total errors: heat + 0.51 per cent., oxygen — 0.51 per cent., carbon dioxid — 0.36 per cent., water + 3.13 per cent. The respiratory quotient averaged 0.666 while the theoretical quotient was 0.6667.

Four normal men and two cardiac patients were studied in the calorimeter lying flat in bed and in the semireclining position propped up with a back rest, or else in a comfortable steamer chair. A total of twenty-one experiments showed that the metabolism averaged 3 per cent. lower in the semireclining posture. One of the cardiacs, and pos-

sibly one of the normal controls, showed a slightly higher metabolism when propped up in bed.

The difference between the results is so small that in the study of pathologic cases we can use the same figures for the average normal metabolism in both postures. In the majority of cases, however, the energy requirement is lower in the orthopneic position.

477 First Avenue.

CLINICAL CALORIMETRY

TWELFTH PAPER

THE METABOLISM OF BOYS 12 AND 13 YEARS OLD COMPARED WITH THE METABOLISM AT OTHER AGES *

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In the period of development of boys, the years immediately preceding puberty are of especial interest. By this time the figure has lost most of its childish characteristics and the mind has reached a point of great intelligence. Although the individual has scarcely passed the half-way mark in the years of growth, and has only attained half his future weight, yet he resembles the adult much more than he resembles the infant. At this stage the sex glands have not yet begun the rapid development of puberty with its profound effect on the whole organism. Curiously enough there is a sudden increase in the rate of growth which takes place at this time. In fact, we may consider boys in the period of prepubescence as individuals of adult form but of small size, growing rapidly, and as yet scarcely influenced by the internal secretions of the sex glands. The study of their respiratory exchanges may throw light on many problems.

Recent developments in the science of metabolism have emphasized the necessity of using, for purposes of comparison, only those experiments in which the subjects were absolutely quiet. Since the assimilation of food increases the metabolism during four or five hours following a small meal, and five to ten hours after a large one, it is important to use only experiments in which this specific dynamic action is either slight or absent. The necessity for absolute quiet has long been recognized by Johansson and the Zuntz school, but has only been fully appreciated elsewhere for the last five years or so. The observations of Rubner[1] and Sonden and Tigerstedt[2] were made before this was understood, and the children were studied in large respiration chambers where they sat fairly quiet in chairs, eating from time to time, or else, as in the case of Rubner's boys, moving about the room at will. This

* Submitted for publication Feb. 4, 1916.

* From the Russell Sage Institute of Pathology, in Affiliation with the Second Medical Division of Bellevue Hospital.

1. Rubner: Beitrage zur Ernährung im Knabenalter, Berlin, 1902.

2. Sonden and Tigerstedt: Untersuchungen über die Respiration und den Gesamtstoffwechsel des Menschen, Skand. Arch. f. Physiol., 1895, vi, 1.

amount of activity might increase the metabolism anywhere from 10 to 30 per cent. above the resting value, and it is obvious that the results can be compared only with those obtained on other individuals who have shown exactly the same amount of muscular movement. It is for this reason that, while the careful work of the above mentioned observers is of great value in showing the changes during the different ages for a given amount of activity, it cannot be used in comparison with the experiments in which the subjects are quiet.

The classical study of Magnus-Levy and Falk[3] established the fact that the metabolism is high during childhood and low after the onset of old age. These observers studied twenty-five children, twelve old men and women and twenty-five of intermediate ages. They used the Zuntz-Geppert apparatus, making several short experiments on each subject in the morning before breakfast, the individual lying at complete rest on a couch. It so happened that they included no boys between the ages of 11 and 14 in their list.

The metabolism during infancy has been well studied by Howland,[4] Schlossmann and Murschhauser,[5] Benedict and Talbot,[6] Murlin and Hoobler,[7] Bailey and Murlin[8] and others,* all of these observers paying especial attention to the question of muscular activity. On account of the difficulty of keeping infants quiet, Benedict and Talbot, and Murlin, Hoobler and Bailey were obliged to feed most of their subjects shortly before the experiment was started. It is quite possible that a lowering of metabolism during sleep may have counterbalanced the slight increase due to the milk ingestion.

All of the above investigators have thrown new light on the subject. It would too greatly extend the bounds of this article to discuss in detail the several excellencies contained in their work. Of special interest is the fact that the metabolism of babies in the first month of life is

3. Magnus-Levy and Falk: Der Lungengaswechsel des Menschen in verschiedenen Alterstufen, Arch. f. Anat. u. Physiol., 1899, Suppl. 315.

4. Howland: Der Chemismus und Energieumsatz bei schlafenden Kindern, Ztschr. f. physiol. Chem., 1911, lxxiv, 1.

5. Schlossman and Murschauser: For references see note 6.

6. Benedict and Talbot: The Gaseous Metabolism of Infants, Carnegie Institution of Washington, Pub. 201, 1914; Studies in the Respiratory Exchange of Infants, Am. Jour. Dis. Child., 1914, viii, 1.

7. Murlin and Hoobler: The Energy Metabolism of Ten Hospital Children, Am. Jour. Dis. Child., 1915, ix, 81.

8. Bailey and Murlin: The Energy Requirement of the New-Born, Am. Jour. Obst., 1915, lxxi, 1.

* Just as this article is going to press Dr. Benedict has kindly called attention to the following reference: Olin: Carbon Dioxid Production in Boys of from 10 to 18 Years of Age; Finska Läksällsk: Handl Helsingfors, 1915, lvii, 1434.

very low. This was apparently first discovered by Hasselbach,[9] and later independently by Murlin,[7] who first brought it to general attention. The same point was shown in Table 7 of Paper 4 of this series.

The metabolism of normal adults has been thoroughly studied in the last few years. Benedict, Emmes, Roth and Smith[10] have collected 157 subjects, some of them as young as 15 years, using chiefly the Benedict universal respiration apparatus. Palmer, Means and Gamble,[11] with the same instrument, have collected a considerable number of normal records and Means[12] has recently calculated his results according to measurements taken by the new surface area formula described in Paper 5[13] of this series. We have also at our command the normal controls of Paper 4[14] and those of Papers 11 and 13, studied in the Sage calorimeter.

All of the above mentioned work on adults was done with very quiet subjects twelve or more hours after the last meal, and the technic of the observers was almost exactly the same. The results of these experiments have been charted in the accompanying curves, together with the work of Magnus-Levy and Falk, of Howland, Benedict and Talbot, Murlin and Hoobler, and Bailey and Murlin for comparison with the new results obtained on the boys 12 and 13 years old. Many other careful workers have studied the normal metabolism, but it has seemed best to use only the above mentioned investigations.

METHOD OF EXPERIMENTS

The Sage calorimeter and the methods employed in this research have been fully described in the previous papers of the series entitled Clinical Calorimetry.[15] The surface area of the boys was determined according to the so-called "Linear Formula" described in Papers 5, 9 and 10. The calories derived from protein were calculated from speci-

9. Hasselbach: Respirations—For søg Paa Nyfødte Dørn, Bibliot. f. Læger, 1904, 8 de Række 5th Bind, 219.

10. Benedict, Emmes, Roth and Smith: The Basal, Gaseous Metabolism of Normal Men and Women, Jour. Biol Chem., 1914, xviii, 139. Benedict and Roth: The Metabolism of Vegetarians as Compared with the Metabolism of Non-Vegetarians of Like Weight and Height, Ibid, 1915, xx, 231. Benedict and Smith: The Metabolism of Athletes as Compared with Normal Individuals of Similar Height and Weight, Ibid, p. 243. Benedict and Emmes: A Comparison of the Basal Metabolism of Normal Men and Women, Ibid, p. 253. Benedict: Factors Affecting Basal Metabolism, Ibid, p. 263.

11. Palmer, Means and Gamble: Basal Metabolism and Creatinin Elimination, Jour. Biol. Chem., 1914, xix, 239.

12. Means: Basal Metabolism and Body Surface, Jour. Biol. Chem., 1915, xxi, 263.

13. Clinical Calorimetry, Paper 5, The Archives Int. Med., 1915, xv. 868, 870.

14. Clinical Calorimetry, Paper 4, The Archives Int. Med., 1915, xv, 835.

15. Papers 1 to 8, The Archives Int. Med., 1915, xv, 793-945; Papers 9 to 17, Ibid., 1916, xvii, 855-1059.

TABLE 1.—RESULTS OF CALORIMETER—

Subject, Date, Weight, Surface Area, Linear Formula	Period	End of Period	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.
F. R. S. .... 3/20/15 32.09 Kg. 1.124 Sq. M.	Prelim.	10:57	.....	.....	.....	.....	.....	......	.....
	1	11:57	19.62	17.43	0.819	28.29	0.456	57.95	63.13
	2	12:57	19.41	16.98	0.831	27.91	0.456	56.65	59.22
	3	1:57	21.10	18.32	0.838	30.54	0.458	61.33	63.33
								175.93	
J. D. D. B. .... 3/26/15 34.52 Kg. 1.224 Sq. M.	Prelim.	11:01	.....	.....	.....	.....	.....	......	.....
	1	12:01	19.21	15.60	0.896	25.33	0.510	52.72	59.65
	2	1:01	19.39	17.89	0.789	25.89	0.510	58.92	64.52
								111.64	
Raymond M. ...... 4/3/15 30.41 Kg. 1.064 Sq. M.	Prelim.	11:14	.....	.....	.....	.....	.....	......	.....
	1	12:14	19.46	17.04	0.830	25.47	0.390	56.99	55.38
	2	1:14	19.81	18.40	0.783	26.35	0.390	60.96	55.90
								117.95	
Reg. F. .... 4/5/15 35.44 Kg. 1.22 Sq. M.	Prelim.	11:01	.....	.....	.....	.....	.....	......	.....
	1	12:01	21.07	16.87	0.908	26.85	0.411	57.55	65.26
	2	1:06	25.87	19.37	0.971	29.66	0.411	66.13	73.41
								123.68	
Harry B. .... 4/6/15 36.57 Kg. 1.232 Sq. M.	Prelim.	11:05	.....	.....	.....	.....	.....	......	.....
	1	12:05	20.97	17.85	0.854	33.11	0.594	59.66	62.59
	2	1:05	20.48	17.03	0.875	32.13	0.594	57.15	62.87
								116.81	
Henry K. .... 4/7/15 35.98 Kg. 1.224 Sq. M.	Prelim.	11:10	.....	.....	.....	.....	.....	......	.....
	1	12:10	20.24	16.38	0.898	26.17	0.251	55.94	60.17
	2	1:10	21.55	18.87	0.831	28.67	0.251	63.39	64.75
								119.33	
Arthur A. .... 4/8/15 30.59 Kg. 1.126 Sq. M.	Prelim.	11:13	.....	.....	.....	.....	.....	......	.....
	1	12:13	17.57	17.01	0.751	21.74	0.308	55.84	59.51
	2	1:13	18.64	16.97	0.799	21.58	0.308	56.46	58.32
								112.30	
Leslie B. .... 4/9/15 28.53 Kg. 1.050 Sq. M.	Prelim.	11:15	.....	.....	.....	.....	.....	......	.....
	1	12:15	19.81	18.16	0.793	24.21	0.437	60.08	56.12
	2	1:15	16.87	14.40	0.852	21.17	0.437	48.21	47.50
								108.29	

—EXPERIMENTS ON BOYS

Direct Calorimetry (Rectal Temp.), Cal.	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M. (Meeh)	
......	37.24	..	..	....	..	..	..	.....	.....	Basal
58.79	37.09	81	15	0.82	21	48	31	1.806	46.62	
59.80	37.11	78	24	0.84	21	43	36	1.765	45.58	
63.30	37.13	80	34	0.85	20	41	39	1.911	49.34	Restless. Excluded from basal averages
181.89										
......	37.56	..	..	....	..	..	..	.....	.....	Basal
55.27	37.42	78	7	0.93	18	26	56	1.527	40.40	
61.02	37.32	76	16	0.78	23	58	19	1.707	45.15	
116.29										
......	36.83	..	..	....	..	..	..	.....	.....	Basal
54.63	36.90	83	5	0.84	18	45	37	1.874	47.49	
56.54	37.21	87	12	0.78	17	62	21	2.005	50.80	
111.17										
......	37.35	..	..	....	..	..	..	.....	.....	Basal
55.34	37.10	78	5	0.94	19	17	64	1.624	43.34	
69.40	36.99	80	20	1.01	17	0	83	1.866	49.80	
124.74										
......	37.30	..	..	....	..	..	..	.....	.....	Basal
59.03	37.18	88	5	0.87	26	33	41	1.632	43.97	
61.19	37.15	89	5	0.90	28	25	47	1.563	42.12	
120.22										
......	37.02	..	..	....	..	..	..	.....	.....	Basal
51.77	36.74	88	5	0.91	12	27	61	1.555	41.65	
67.20	36.83	87	7	0.83	11	52	37	1.762	47.20	
118.97										
......	36.89	..	..	....	..	..	..	.....	.....	Basal
54.24	36.69	81	11	0.74	15	75	10	1.825	46.38	
58.88	36.72	82	4	0.80	14	58	28	1.846	46.89	
113.12										
......	37.46	..	..	....	..	..	..	.....	.....	Basal
55.40	37.44	..	10	0.79	19	58	23	2.106	52.24	
44.53	37.33	88	5	0.87	24	34	42	1.690	41.92	
99.93										

mens voided between the hours of 9 a. m. and 1:15 p. m. Twenty-four-hour specimens could not be secured.

The subjects of the experiments here discussed were all healthy, normal boys between their twelfth and fourteenth birthdays. Two of them, F. R. S. and J. D. D. B., were related to members of the calorimeter staff, the others were Boy Scouts from one of the suburbs. A month or so before the research had been planned the writer had given the required physical examination to a group of sixteen Boy Scouts. The scout master selected as subjects for the experiments the five who most needed to earn money for uniforms. Harry B. was chosen because he was a patrol leader and able to manage the other boys. All the eight boys lived in the suburbs except J. D. D. B., who was home on a vacation from boarding school. They were all bright mentally and active physically, apparently being in constant motion when not studying or sleeping. The urine was examined in all cases and found to be normal.

In order to accustom the boys to the apparatus, they were brought to the calorimeter room a week or so before the experiment, sealed in the apparatus for a short time and trained in the simple routine. This was omitted in the case of F. R. S., who had helped his father build parts of the machine and was thoroughly familiar with the work. All of the boys considered the adventure as a lark and not one was apprehensive. A small breakfast, consisting of an egg, a slice of toast and a glass of milk, was allowed them at 7 o'clock, because it seemed probable that boys of this age would be ravenous and irritable if sent in from the country in a fasting condition.

The problem of keeping the youngsters quiet for three hours was hard to solve. It seemed best to allow them to read for one of the hours in a small book with large print. This proved satisfactory, the work involved in holding the book and turning the pages was very small. During the rest of the time the boys were bored. F. R. S. and J. D. D. B. remained quiet for two hours, but the former was so restless in the third period that experiments of this length were not attempted again. For the six Boy Scouts another expedient was tried. All the boys were anxious to earn pocket money and all were liberally paid for the experiments. A system of fines was instituted and the boys were told that one cent would be withheld for each centimeter that the work-adder tallied above 15 per hour. This figure was arbitrarily selected since it represents the average activity of a quiet subject who turns over once or twice an hour and shifts his position a few times to make himself comfortable. The boys took good care not to approach the danger mark. After the fine system was started the 15 centimeter mark was exceeded in only one period, and the lads as a group were the quietest of subjects.

TABLE 2.—SUMMARY OF EXPERIMENTS ON BOYS

Name	Age		Weight, Kg.	Height, Cm.	Circumference of Thorax, Cm.	Signs Approaching Puberty	Surface Area, Sq. Meters		Calories per Kg. per Hr.	Meeh's Formula		Linear Formula		Average R. Q.	Average Pulse
	Years	Mos.					Meeh's Formula	Linear Formula		Calories per Sq. Meter per Hr.	Per Cent. above Adult Aver., 34.7	Calories per Sq. Meter per Hr.	Per Cent. above Adult Aver., 39.7		
J. D. D. B.	12	2	34.52	152.8	67.8	+	1.305	1.224	1.62	42.8	23	45.6	15	0.84	77
Leslie B.	13	3	28.53	140.8	61.8	±	1.150	1.050	1.90	47.1	36	51.6	30	0.82	88
Raymond M.	12	7	30.41	140.5	65.8	0	1.200	1.084	1.94	49.1	42	54.4	37	0.81	85
Reginald F.	12	8	35.44	148.2	68.2	+	1.328	1.220	1.75	46.6	34	50.7	28	0.94	79
F. R. S.	12	10	32.09	141.5	66.2	0	1.243	1.124	1.79	46.1	33	51.0	29	0.83	80
Arthur A.	13	8	30.59	146.6	65.4	0	1.204	1.126	1.84	46.6	33	49.9	26	0.78	81
Harry B.	13	10	36.57	146.0	71.4	++	1.357	1.232	1.60	43.0	24	47.4	19	0.86	88
Henry K.	13	11	35.98	148.2	67.7	±	1.343	1.224	1.66	44.4	28	48.8	23	0.86	87
Average............	..	..	.....	.....	....	..	.....	.....	1.76	45.7	32	49.9	26	0.84	83

The question may be raised as to whether or not the breakfast taken by the subjects between 7 and 7:30 a. m. increased the metabolism between the hours of 11 and 1 o'clock. The standard meal allowed consisted of 1 egg, 1 glass of milk and 1 slice of toast with butter. They were shown standard portions of these and copied them as closely as possible, except Arthur A., who took nothing but 1 egg. The meal contained approximately 17 gm. of protein, 22 of fat and 30 of carbohydrate, with about enough calories to maintain a boy 5½ hours, if we allow an increase of 20 per cent. over the basal metabolism, to cover the journey to the hospital. J. D. D. B., who took his breakfast half an hour later than the others, had the lowest metabolism and Arthur A., who took the smallest breakfast, had almost the highest heat production. Mr. H. L. Higgins of the Nutrition Laboratory in Boston, kindly made a series of observations on a young man who took this same breakfast and found that the metabolism returned to its fasting level 3½ hours after the meal. It may perhaps be said that the metabolism was increased by the ride of fifty minutes in the train, ten minutes in the street cars and the walk of five minutes. The boys all reached the hospital by ten minutes past 9, sat in a chair for three fourths of an hour, undressed and lay on the bed within the calorimeter at about 10 o'clock, the experiment beginning at 11, or three and one half to four hours after breakfast. It will be noted that there was no significant drop in pulse rate or metabolism in the second periods. It is exceedingly doubtful if the combined increase due to the previous exercise, the specific dynamic action of food and the quiet reading amounted to 5 per cent. above the fasting level at absolute rest.

DESCRIPTION OF SUBJECTS

F. R. S., 12 years and 10 months old. He has been perfectly well except for one attack of abdominal pain in 1911, diagnosed as appendicitis.

Physical Examination.—Short, muscular and unusually well built; no signs of approaching puberty; disposition very active.

This boy was the son of the laboratory technician, who built and still operates the calorimeter, and he was thoroughly at home in his surroundings, having in fact helped to make the bed on which he lay. He was the only boy placed in the calorimeter for an experiment without previously staying for a short period in the apparatus. On the morning of the observation he took the standard breakfast at 6:40 a. m. While in the calorimeter he read quietly for the first hour. In the second hour he tried to sleep and was somewhat restless for part of the time. In the third hour he read for five minutes, and during the remainder of the time was so restless that this period has been excluded from the averages.

J. D. D. B., aged 12 years, 2 months. In 1911 he had measles; about six months prior to the experiment he suffered from a number of furuncles in the outer ear, and two weeks before the experiment had a cold in the head which lasted four days.

Physical Examination.—Very tall for his age, complexion dark, bones long and not heavy, very little subcutaneous fat, muscles sinewy; temperament rather

high-strung but under good control; genitalia just beginning to develop; there were a few pubic hairs; voice not yet affected.

On the morning of the experiment he took the standard breakfast at 7:45 a. m., and came to the hospital in the street cars, being the only boy who lived in the city. In the first hour he was almost motionless and slept for a short time, and in the second period he read quietly in a small book.

Raymond M., aged 12 years, 7 months. He remembers that he had whooping cough as a baby and that he had measles two years previous to the experiment. He is short, stocky and muscular, but the thorax is rather narrow with a prominent sternum. His complexion is light and his disposition quiet. His physical examination is normal except that the right tonsil is moderately enlarged. He shows no signs of approaching puberty.

On the morning of the experiment he took the standard breakfast at 7:30 a. m. During the first period he read very quietly and in the second period tried to sleep.

Reginald F., aged 12 years, 8 months. He remembers no illnesses except measles; he is tall, slim, of graceful build; his hair is brown; the pubic hair is just making its appearance and his voice suggests slight change; both mammary glands are palpable, measuring about 10 by 2 mm. The left gland is slightly tender.

Standard breakfast at 7:15 a. m. In the first period he was very quiet, reading for twenty minutes. In the second period he slept for twenty minutes but was restless during the remainder of the time.

Harry B., aged 13 years, 10 months. Born in England; has been in this country eleven years; had measles in childhood and two weeks before the experiment was sick in bed a couple of days with stomachache. The day before he noticed a slight infection of his finger which pained him until it discharged a little pus. On the day of the experiment it did not hurt and he felt perfectly well.

Physical Examination.—Of moderate height and stocky muscular build, with broad shoulders; complexion fair. The left forefinger is red and slightly swollen near the nail, but there is no redness up the arm and no tenderness or swelling of the axillary nodes. The genitalia are approaching the adult type in development and there is a scant growth of pubic hair, and the mammmary glands are just palpable. The voice has not yet started to change.

He took the standard breakfast at 7:15 a. m. During the first hour he was awake but very quiet, and in the second hour he was also quiet, reading for thirty minutes.

Henry K., aged 13 years 11 months. Does not remember any illnesses except measles. He is tall, fairly muscular and well built except for the chest, which is narrow, with a prominent sternum. The upper jaw is narrow with high arch and prominent incisor teeth. His complexion is fair, his disposition quiet. The only sign of approaching puberty is a scant growth of pubic hair.

He ate the standard breakfast at 7 a. m. In the first hour of the experiment he was practically motionless and in the second hour was very quiet, reading for fifty minutes.

Arthur A., aged 13 years, 8 months. Thinks he had measles and mumps when 3 or 4 years of age; three years prior to the experiment he broke his femur in a coasting accident. There is now no shortening of the limb. He is of slight, sinewy build with well formed chest, but gives the impression of being somewhat undernourished; complexion fair, disposition rather nervous; no signs of approaching puberty.

The evening before the experiment he was taken, with the other Boy Scouts, to an exhibition drill and in the excitement took no supper except one bun at 5 p. m. On the morning of the observation in the calorimeter he ate nothing but an egg at 7 a. m. He was very quiet both hours, reading forty minutes in the second period.

Leslie B., brother of Harry B., aged 12 years, 3 months. In childhood he had measles and chickenpox. For the last few months he has had no appetite for breakfast and had suffered from stomachaches. He is of small frame, rather thin and undernourished but his color is good and his muscles strong. His complexion is fair and his disposition bashful and quiet. His teeth are in poor condition and his tonsils are enlarged. In the abdomen several masses of constipated feces are palpable. The only sign of approaching puberty is a scant growth of pubic hair.

On the morning of the experiment he took the standard breakfast at 7 a. m. In the first period he was quiet, reading for forty-five minutes. In the second period he was unusually quiet, sleeping about three-quarters of the time. He was perfectly well until he came out of the calorimeter. He then felt faint, but recovered quickly.

DISCUSSION OF RESULTS

The total heat production in the eight experiments as measured by the method of indirect calorimetry was 985.93 calories, by the method of direct calorimetry 986.33 calories, a difference of 0.04 per cent.

A summary of the results obtained on the boys will be found in Table 2. It will be noted that the metabolism averaged 32 per cent. above the adult figure per unit of surface area according to Meeh's formula, or 25 per cent. above according to linear figure. The true significance of these results can be appreciated only if we consider the variations in the intensity of metabolism from birth to old age. It is for this reason that the results on normal individuals have been grouped in Charts 1 to 3. The first (Chart 1) represents the metabolism from birth to the age of 24 calculated per *kilogram of body weight*. It will be noted in general that the heat production of the infants shows wide variations, but at a much higher level than that of the adults. A uniform decrease in the metabolism becomes evident after the sixth year, becoming less marked after the twentieth year. In Paper 4 of this series we have mentioned the disadvantages of using the body weight as a basis of comparison of individuals of different sizes. Small animals show per kilogram a calorific production so much greater than that of large animals that it is almost a waste of time to compare children and adults by using this standard. For clinical purposes, however, the body weight is a convenient guide.

Chart 2 shows the metabolism from birth to the age of 24 expressed in terms of calories per square meter of body surface as determined by Meeh's formula. Lines have been drawn showing as nearly as possible the averages for males and females. It will be seen that the metabolism is low at birth, increases rapidly during the first year, reaches its maximum in the almost unexplored period between the ages of 1 and 6, falls quite rapidly until the age of 20, then very slowly. During infancy there is no apparent difference between the sexes, but after the age of 6 the girls and women have a distinctly lower metabolism.

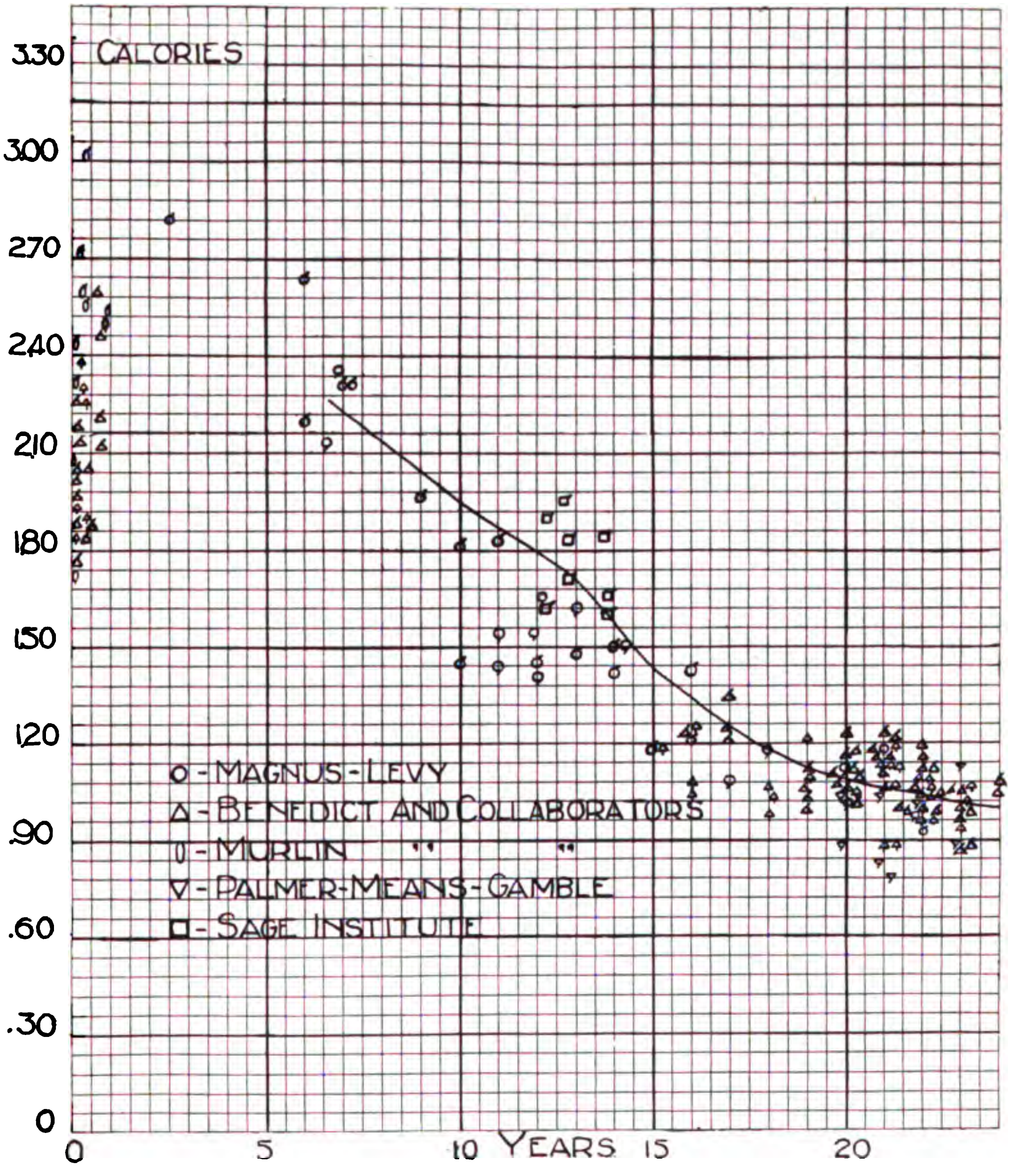
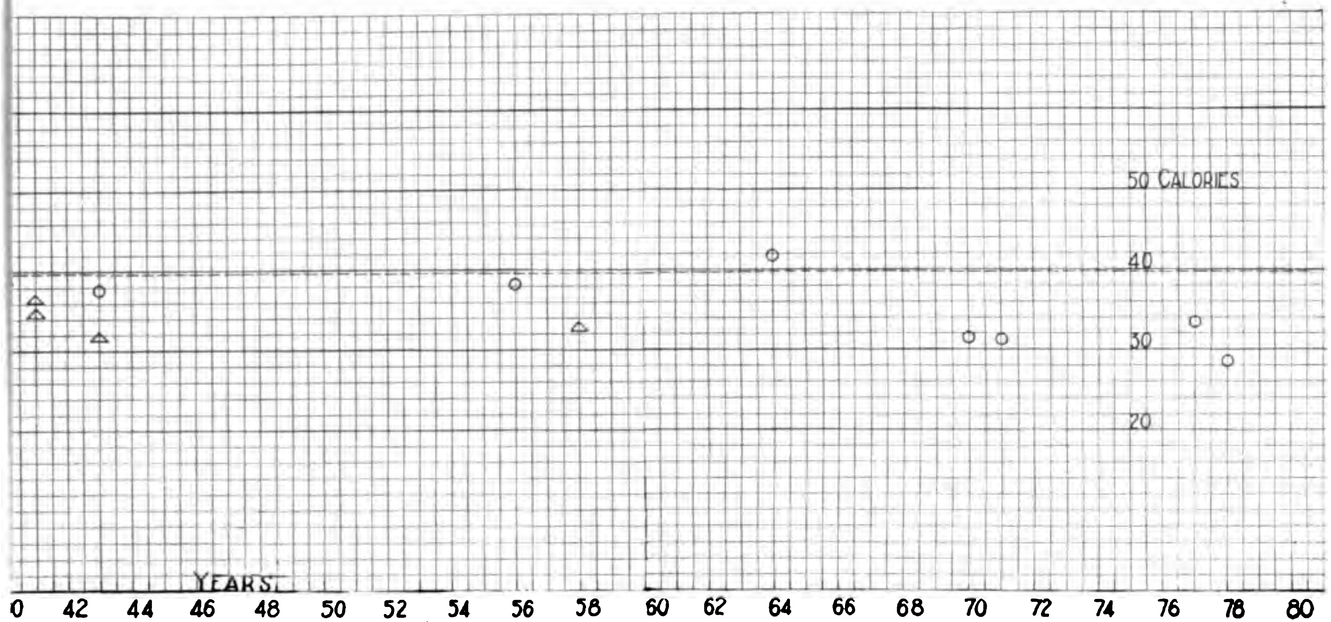


Chart 1.—Variation of basal metabolism with age: Calories per hour per kilogram of body weight.

In Papers 4 and 5 we have shown the reasons for preferring the calories per unit of surface area as a guide for the intensity of the metabolism, and have also shown the errors and limitations of Meeh's formula which has been the standard for so many years. The fact that the formula shows an average plus error of 16 per cent. scarcely affects its value for purposes of comparison with subjects of usual build. On the other hand, the tendency of this error to be much smaller in the case of thin subjects and larger in the case of fat ones, is of considerable importance. New-born infants are relatively thin, older children relatively chubby until the age of 4 or 5, when they grow taller and thinner until puberty. Women tend to put on weight after 30 and men do so five or ten years later. If, therefore, we try to correct the curve for these errors in Meeh's formula we find that the peak in early childhood will be accentuated and the rest of the curve flattened out.

Chart 3 gives the results for males expressed in terms of calories per square meter of body surface as determined by the new so-called "Linear Formula." It will be seen that the metabolism of the adults is somewhat more uniform and that the boys average only 25 per cent. above the adult level instead of 32 per cent. as in the previous chart. This indicates a true increase of 25 per cent. above the heat production which a group of normal adults would show if they were the same size as the boys. For purposes of comparison the metabolism of the infants has been recorded in terms of Lissauer's Formula.[18]

When we consider the question of the metabolism in the first year or so of life we must remember that the infant differs greatly from the adult in the proportions of the body and the relative size of the various organs. A baby 5½ feet tall would be a short legged, long bodied monster with an enormous head. He would have a very large liver and a comparatively large thyroid gland. At birth the liver comprises 4.5 per cent. of the body weight and during adult life less than 3 per cent. Since this is supposed to be a gland of high metabolic activity, one would naturally expect an increased heat production in an organism with a relatively large liver. Still more important in regulating metabolism is the thyroid gland, which is considered to be three times as large in the new-born as in the adult, although recent measurements by Parski makes the figures somewhat smaller. Thyroid secretion has such a marked effect on development that it is quite possible that the gland is relatively more active in childhood. Some might even argue that the increased metabolism of this period is in itself evidence of a greater activity of the thyroid. Such a theory would be unwarranted unless supported by a greater number of facts than are now available. It should be remembered that the phenomena of growth are not so very different with invertebrates which have no thyroids.



per hour per square meter of body surface—Linear formula.

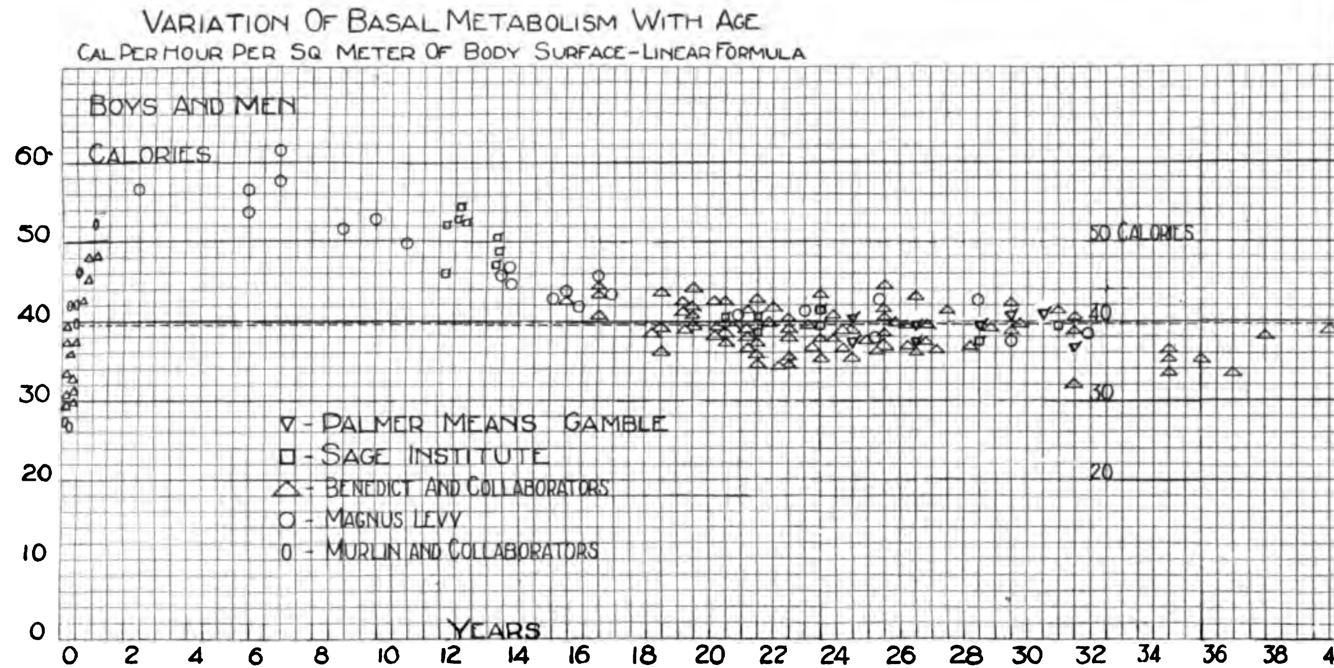


Chart 3.—Variation of basal metabolism with age; Calories

The Sage calorimeter has recently been able to throw an interesting sidelight on the relationship of body form to metabolism. Two men who in youth had lost both legs in accidents, were studied in the respiration chamber and the surface area determined by formula and actual measurement. The one who was fat showed a metabolism only 4 per cent. above the normal average; the one who was muscular was 2 or 3 per cent. above. These men resembled infants in the relative proportion of body to extremities. This indicates that the law of surface area holds true under dissimilar physiological conditions such as are found in legless men. The high metabolism of infants is not therefore, due to the differences in body shape and body composition.

These factors are almost entirely ruled out in the case of the boys 12 and 13 years old. At this age the body has assumed almost the adult proportions and the liver and thyroid are not much larger in proportion to the body weight than in later life. The metabolism of these boys is very much higher than that of adults. It is rather a striking fact that the metabolism was distinctly higher in the boys who showed no signs of approaching puberty than in those who showed traces of pubic hair and increasing development of the genitalia. It is hoped that the same group of boys can be studied at intervals during pubescence. These boys can be compared with the case of infantilism studied by McCrudden and Lusk in the calorimeter of the Department of Physiology of the Cornell Medical College. This dwarf, who was 17 years old, and about the size of an average boy of 6 years, showed a metabolism of 23.3 calories per hour per square meter (Meeh), which was 7 per cent. below the adult normal average.

The growth of children in length and weight is very rapid during the first two years of life and then decreases somewhat between the ages of 8 and 12. Following this is a period of increased growth, with relatively greater gain in stature than in weight. This begins in almost all the nations at the age of 12 or 13 in boys and reaches its height between the thirteenth and fifteenth years. The figures of Boas[16] and Burk[17] are well worth consulting, and Wiener's[18] measurements of three of his sons show this increase in the period of prepubescence very clearly. The curve of weight is somewhat different, since boys become relatively thinner as they grow tall and do not fill out again

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16. Boas: The Growth of Toronto Children, Report U. S. Commr. Education, 1896-97, ii, 1541.
17. Burk: Growth of Children in Height and Weight, Am. Jour. Psychol., 1898, ix, 253.
18. Wiener: Das Wachstum des menschlichen Körpers, Karlsruhe, 1890.
Chart reproduced in Burk's paper (note 17) and also in Hall's Adolescence, New York, 1904.

until puberty is well established. In the case of girls the period of increasing growth comes a year or two earlier.

In adult life the nearest approach to the growth of childhood is found in the period of convalescence from acute infectious diseases. The fact that the metabolism is increased at such times was demonstrated by Svenson, Rolly and others. Coleman and Du Bois[19] have shown that after typhoid the metabolism which falls to normal at the end of the fever, may rise to an average of 17 per cent. above normal in the second and third weeks of convalescence. It is significant that the body which is repairing the losses of protein and fat during the fever should be maintaining its metabolism at a level which approaches that found in childhood. It is also significant that a second peak in the curve representing the heat production at different ages is found in the case of these boys just at the period of a renewed increase in the rate of growth. The evidence points toward a specific increase in the metabolism of the growing organism.

There is no apparent explanation for the fact that the metabolism was higher in the boys who showed no signs of approaching puberty than in the others. It is difficult to explain the low metabolism of newborn infants. It must be considered, however, that the unborn baby is essentially similar to an internal organ which is practically free from the play of external physical stimuli. Under such conditions the heat production must be on a different level from that in later life after a fuller development of the neuromuscular elements has been completed.

SUMMARY AND CONCLUSIONS

Eight normal boys, 12 or 13 years old, were studied in the respiration calorimeter four to six hours after a small breakfast. They were allowed to read for one of the two experimental hours, but were very quiet. The methods of direct and indirect calorimetry agreed within 0.04 per cent. Their heat production per unit of surface area was 32 per cent. higher than the adult level according to Meeh's formula, or 25 per cent. higher according to the more accurate "Linear Formula."

In studying the effect of growth on metabolism, interpretation of the results obtained on infants is complicated by the fact that babies differ greatly from adults in the proportions of the body and the relative size of the viscera, notably the liver and thyroid. Boys just before the onset of puberty have almost adult proportions. They are in the midst

19. Coleman and Du Bois: The Influence of the High Calory Diet on the Respiratory Exchanges in Typhoid Fever, The Archives Int. Med., 1914, xiv., 168; also Clinical Calorimetry, Paper 7, ibid., 1915, xv., 887.

of a period of accelerated growth. The fact that the metabolism is high, points to a specific increase in the metabolism of the growing organism.

The writer wishes to thank those whose assistance made this research possible. The electrical measurements were made by Mr. F. G. Soderstrom, the residual analyses and calculations by Dr. A. L. Meyer and the calculations were checked by Miss Grace Sims. Urinalyses were made by Mr. F. C. Gephart and Mr. R. H. Stone.

CLINICAL CALORIMETRY

THIRTEENTH PAPER

THE BASAL METABOLISM OF NORMAL ADULTS WITH SPECIAL REFERENCE TO SURFACE AREA*

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NEW YORK

Since the writing of Paper 4[1] of this series an unusual amount of work has been published on the subject of the normal metabolism. It is now possible to calculate the normal baseline much more exactly than a year ago and it is therefore necessary to reconsider the whole question at this early date. The figures representing the average normal metabolism have been changed frequently since the study of the respiratory exchanges began and it may be said that the chief advance has depended on the fact that it has been possible to make the variation in the normal smaller and smaller each year. With the oldest type of large respiration chamber the range of heat production fluctuated enormously with the uncontrolled influences of muscular activity and the specific dynamic action of food. With the improved technic of Johansson and with the small apparatus of the Zuntz school these factors were eliminated, but errors due to changes in the calorific factors for O_2 and CO_2 remained. The normal variation was frequently quoted as from about 2.5 to 5.0 c.c. O_2 per kilogram and minute with a mean of about 3.5 c.c. Under these conditions a pathological departure from the average normal as great as 40 per cent. might be obscured. In 1914 Coleman and Du Bois[2] gathered 48 controls from various sources including seven studied in the Sage calorimeter and gave the figure 34.2 calories per hour as the average heat production per square meter of body surface as determined by Meeh's formula. They pointed out that the normal variation was only plus or minus 10 per cent. if the surface area were used as a standard. In Paper 4 of this series,[1] on the basis of a much larger number of controls, we selected the average

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* From the Russell Sage Institute of Pathology, in affiliation with the Second Medical Division of Bellevue Hospital.

1. Gephart and Du Bois: Clinical Calorimetry, Paper 4, The Archives Int. Med., 1915, xv, 835

2. Coleman and Du Bois: The Influence of the High Calory Diet on the Respiratory Exchanges in Typhoid Fever, The Archives Int. Med., 1914, xiv, 168.

figure of 34.7. Since then Benedict, Emmes, Roth, and Smith[3] have published the details and have discussed their experiments which were only briefly reported at the time of our last publication. They found the metabolism of vegetarians to be practically the same as that of nonvegetarians, while the athletes average 7 per cent. higher than the nonathletes used as controls. This is accounted for in part by the fact that the athletes were somewhat younger than the controls with whom they were compared. The average age of the fifteen athletes was 22⅓ years and the average heat production 40.7 calories per square meter per hour as recalculated according to the height-weight chart. This is only 2.5 per cent. higher than our standard for normal men. Benedict and his co-workers have pointed out the fact that the younger subjects show a higher metabolism and that the heat production is much lower when the subject is asleep at night than when he is awake in the day time. They have found the metabolism of women average about 6 per cent. lower than that of men. The extremes of variation in the oxygen consumption of the same man over the course of months and years are shown in a very instructive table of thirty-five subjects. Eleven show a variation less than 10 per cent., eighteen show from 10 to 20 per cent. and six a difference of 20 to 31 per cent., the average variation being 13.9 per cent. It must be remembered that this table shows the extremes, giving the percentage increase of the very highest period over the very lowest. The results in an early morning period when the subject was asleep may be contrasted with an afternoon period when he was awake and weary of experimentation. The "Universal" respiration apparatus with which these tests were made can be used only for periods of 10 to 20 minutes and with some people there may be a considerable amount of discomfort from the mouth or nose pieces. On the whole it is quite remarkable that the extremes of variation are not greater. It is to be hoped that the details of this table will be published so that we may estimate the frequency with which observations under similar conditions show results which differ materially from the average. Benedict also calls attention to the variation of the metabolism of different individuals according to body weight and surface area.

Palmer, Means and Gamble[4] have studied a considerable number of normal men and women and have found that the creatinin elimination bears a constant relationship to the basal heat production. Means[5] has

3. Benedict, Emmes, Roth and Smith: Jour. Biol. Chem., 1914, xviii, 139. Benedict and Roth: The Metabolism of Vegetarians as Compared with the Metabolism of Non-Vegetarians of Like Weight and Height, ibid, 1915, xx, 231. Benedict and Emmmes: A Comparison of the Basal Metabolism of Normal Men and Women, ibid, xx, p. 253. Benedict and Smith: The Metabolism of Athletes as Compared with Normal Individuals of Similar Height and Weight, ibid., xx, p. 243. Benedict: Factors Affecting Basal Metabolism, ibid, xx, p. 265.

4. Palmer, Means and Gamble: The Basal Metabolism and Creatinin Elimination, Jour. Biol. Chem., 1914, xix, 239.

5. Means: Basal Metabolism and Body Surface, ibid, 1915, xxi, 263.

calculated out the metabolism of these same subjects according to square meters of body surface as determined by Meeh's formula and by the new linear formula described in Paper 5 of this series. The average figure for men according to Meeh's formula was 33.2 calories per hour, according to the "Linear Formula" 39.6. The averages for women were lower, Meeh's formula 29.9, "Linear Formula" 38.2. The greatest variation from the average was 12.3 per cent. according to Meeh's formula and 7.9 per cent. according to the linear, the mean variations were 4.8 per cent and 4 per cent., respectively. Means[6] has also shown that the apparent depression of metabolism in obesity in most cases was due to the large plus error in Meeh's formula, and that according to the linear formula his two very stout subjects came within normal limits.

In Papers 5 and 9 in this series attention has been called to the variable plus error in Meeh's formula, which averages about 15 per cent., and a formula based on linear measurements has been described. In Paper 10 a "Height-Weight" formula is given which makes it possible to determine the approximate surface area of subjects described in publications in which the height and weight are stated. Results expressed in terms of square meters of surface area are comparable if either the linear formula or "Height-Weight Formula" be used, but are about 15 per cent. higher than if Meeh's formula be applied. This necessitates the use of two different sets of figures to represent the average metabolism of men between the ages of 20 and 50—39.7 calories per square meter per hour according to the linear formula, 34.7 calories according to Meeh's formula. In Paper 11 it is shown that the metabolism is slightly lower in the semireclining posture than flat in bed. In Paper 12 the increase in metabolism during the period of growth is discussed in detail.

METHODS AND SUBJECTS

The methods described in Paper 4 of this series were followed in the present work. Many of the subjects have been reported in previous papers.

Morris S., former typhoid patient, is reported in Paper 6 where the history and experimental data are given. At the date of the experiments here discussed he was in perfect health. Dec. 17, 1914, a basal determination was made and the next day between 8:40 and 9:20 a. m. he ate the protein meal, consisting of 110 gm. egg white, 21 gm. egg yolk, 600 c.c. fat-free milk, 150 gm. pot cheese and 10 gm. lactose. This according to analysis of the cheese and milk contained 9.6 gm. nitrogen. He was quiet throughout the experiment and during the third hour slept for forty minutes. The metabolism was much lower during this hour and it should be excluded from the averages.

Albert G. Normal control whose history is given in Paper 12. Dec. 30, 1914, he was given 79 gm. olive oil at 10:15 a.m. During the first and second periods

6. Means: Studies of the Basal Metabolism in Obesity and Pituitary Disease, Jour. Med. Research, 1915, xxvii, 121.

he slept fourteen and ten minutes, respectively. Jan. 4, 1915, at 10:13 a.m. he was given 115 gm. commercial glucose, the equivalent of 100 gm. pure dextrose. He slept most of the first period. In the third period the CO_2 and O_2 measurements were lost. The experiment was repeated two days later.

A. P. C., normal control, male, 24 years old, 179.4 cm. tall; medical student in good health.

Jan. 21, 1915, after having been on a low nitrogen diet for several days a basal determination was made.

R. H. S. history in Paper 12.

E. F. B. D. history in Papers 4 and 12.

Emma W., normal control. History in Paper 9. She was in unusually good health and was able to take violent exercise. Her menses were regular and not profuse. On examination of the heart there was a marked respiratory allorrhythmia and also an ocasional premature systole. Several electrocardiographic plates were taken but no abnormal beats photographed, although it was possible to see the typical large diphasic swing of the shadow several times. The first experiment was made May 13, which was the second day of the catamenia. To control this factor a second basal determination was made May 17, the third day after the flow had ceased. She was almost motionless both days while in the calorimeter.

AVERAGE BASAL METABOLISM OF MEN

In Paper 4 the results of respiration experiments on 96 men were considered. To this group may be added the nine men of Palmer, Means and Gamble and the four men studied in the Sage calorimeter, Morris S., Albert G., R. H. S., and A. F. C. If we tabulate the results according to the surface area as determined by Meeh's formula there is no need to change the conclusions expressed in Paper 4. The average of the new cases is 33.6 calories per square meter per hour as opposed to the former figure of 34.7. It does not seem necessary to change the base line again. The greatest variation from the mean is 12.3 per cent. as mentioned previously.

In Paper 4 of this series the results in five cases are given in terms of calories per square meter as determined by the new "Linear Formula." Adding the four new cases of this paper we have a total of nine normal men whose surface area has been accurately measured. The average basal metabolism is 39.7 calories per square meter per hour ("Linear Formula"). The extremes of variation from the average are + 4 per cent. and — 6 per cent. John L., who was 44 years old, could not be found and measured. His results would probably have been further from the average. Means,[5] who measured his nine subjects by the same method, obtained an average figure of 39.6. Until we have a larger number of subjects measured in this manner the figure 39.7, given above, will be considered the standard with which all results are to be compared.

The results obtained by Benedict, Emmes, Roth and Smith may also be recalculated by means of the new "Height-Weight" chart. If we take the seventy-nine men between the ages of 20 and 50, who were of average body shape, and calculate the calories per square meter per

TABLE 1.—DATA OF—

Subject, Date, Weight, Surface Area, Linear Formula	Period	End of Period	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.
Albert G. .... 12/30/14 64.91 Kg. 1.657 Sq. M.	Prelim.	11:15	.....	.....	.....	.....	.....	......	.....
	1	12:15	23.94	21.20	0.821	30.81	0.418	70.78	74.34
	2	1:15	22.70	20.31	0.813	29.14	0.418	67.63	73.41
	3	2:15	25.40	21.21	0.871	30.47	0.380	71.81	73.78
	4	3:15	24.37	22.30	0.795	30.84	0.380	74.07	74.99
								284.19	
Albert G. .... 1/4/15 65.64 Kg. 1.665 Sq. M.	Prelim.	11:12	.....	.....	.....	.....	.....	......	.....
	1	12:13	29.97	23.79	0.916	31.69	0.445	81.53	81.87
	2	1:12	29.29	20.73	1.03	29.44	0.445	72.45	77.98
								153.98	
Albert G. .... 1/6/15 66.16 Kg. 1.671 Sq. M.	Prelim.	11:11	.....	.....	.....	.....	.....	......	.....
	1	12:11	32.55	22.59	1.05	30.38	0.509	79.19	77.67
	2	1:11	30.64	22.69	0.982	35.28	0.509	78.72	85.06
	3	2:11	29.03	21.73	0.972	33.60	0.509	75.20	77.63
	4	3:11	24.90	22.03	0.822	34.77	0.509	73.54	81.22
								306.65	
A. F. O. .... 1/21/15 69.22 Kg. 1.792 Sq. M.	Prelim.	8:48	.....	.....	.....	.....	.....	......	.....
	1	9:48	24.17	21.28	0.826	27.28	0.261	71.51	73.07
	2	10.48	23.19	20.33	0.830	27.49	0.261	68.44	72.90
								139.95	
Emma W. .... 5/13/15 57.38 Kg. 1.64 Sq. M.	Prelim.	10.41	.....	.....	.....	.....	.....	......	.....
	1	11:41	18.22	16.44	0.806	31.75	0.402	54.60	59.93
	2	12:41	18.41	16.18	0.827	29.11	0.402	53.94	56.21
								108.54	
Emma W. .... 5/17/15 57.26 Kg. 1.64 Sq. M.	Prelim.	11:00	.....	.....	.....	.....	.....	......	.....
	1	12:00	18.55	16.06	0.840	29.15	0.214	54.18	50.86
	2	1:00	18.86	16.77	0.818	27.93	0.214	56.21	52.26
								110.39	

hour, we obtain the figure 38.9. While this figure is slightly lower than ours, it must be remembered that it was obtained by means of the Benedict apparatus with periods only fifteen to twenty minutes long. For these periods the subjects can remain absolutely motionless, something impossible in calorimeter experiments two to four hours long. It seems preferable to use the average normal obtained in the calorimeter as a standard for pathological cases studied in the same apparatus.

—CALORIMETER EXPERIMENTS

Direct Calorimetry (Rectal Temp.), Cal.	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M. (Meeh)	
......	37.00	..	..	....	..	..	..	.....	.....	Olive oil, 79 gm. 10:15 a. m.
69.29	36.91	57	12	0.82	16	52	32	1.090	35.59	Asleep 10 min.
79.53	37.03	61	7	0.81	16	54	30	1.042	34.00	Asleep 10 min.
61.51	36.83	64	10	0.88	14	35	51	1.106	36.10	Awake
74.68	36.84	62	13	0.79	13	62	25	1.141	37.24	Awake
285.01										
......	36.88	..	..	....	..	..	..	.....	.....	Commer. glucose, 115 gm.; water, 200 c.c., 10:13 a.m.
94.63	37.12	65	7	0.94	15	17	68	1.242	40.73	Asleep
72.76	37.03	59	17	1.08	16	0	84	1.104	36.35	Awake
167.39										
......	36.94	..	..	....	..	..	..	.....	.....	Com. glu., 115 gm.; lemon juice, 10 c.c.; water, 125 c.c. at 10:11 a. m.
74.57	36.89	66	11	1.11	17	0	83	1.197	39.32	Quiet
84.19	36.88	64	29	1.02	17	0	83	1.190	39.09	Quiet
75.70	36.85	..	30	1.01	18	0	82	1.137	37.34	Restless
72.69	36.70	57	15	0.83	18	47	35	1.112	36.51	Fairly quiet
307.15										
......	36.89	..	..	....	..	..	..	.....	.....	Basal; low nitrogen diet
61.25	36.69	68	30	0.83	10	52	38	1.033	34.45	Restless
60.55	36.48	74	20	0.84	10	70	20	0.989	32.97	Restless
121.80										
......	37.04	..	..	....	..	..	..	.....	.....	Basal; 2d day of catamenia
54.38	36.93	60	2	0.81	20	52	28	0.952	29.80	Almost motionless
49.73	36.80	58	6	0.83	20	46	34	0.940	29.44	Almost motionless
104.11										
......	36.91	..	..	....	..	..	..	.....	.....	Basal
46.26	36.82	57	4	0.85	10	46	44	0.946	29.61	Almost motionless
55.75	36.90	55	4	0.82	10	55	35	0.982	30.72	Almost motionless
102.01										

If we apply the "Height-Weight Formula" to the averages of the 68 women given by Benedict and Emmes[7] on page 256, we find that the approximate surface area for the average weight of 54.5 kg. and average height of 162 cm. is 1.57 sq. meters. This would make their average heat production per hour 35.9 calories per sq. meter, and if

7. Benedict and Emmes: A Comparison of the Metabolism of Normal Men and Women. Jour. Biol. Chem. 1915, xx, 253.

TABLE 2.—SUMMARY OF RESULTS WITH NORMAL SUBJECTS (ALL MEN EXCEPT EMMA W.)

Name	Age, Years	Average Weight, Kg.	Height, Cm.	Sq. M. Surface Area: Meeh's Formula	Sq. M. Surface Area: Linear Formula or Measured	According to Meeh's Formula: Cal. per Sq. M. per Hour	According to Meeh's Formula: Variation from Average, per Cent.	According to Linear Formula: Cal. per Sq. M. per Hour	According to Linear Formula: Variation from Average, per Cent.
Morris S.	22	61.21	164.3	1.912	1.644	35.2	+1	41.2	+ 4
Albert G.	24	65.90	162.2	2.009	1.667	34.3	—1	41.2	+ 4
R. H. S.*.....	21½	64.36	184.2	1.977	1.830	34.6	—0	37.4	— 6
E..F. D. B. ..	33	74.64	179.2	2.183	1.906	32.9	—6	37.7	— 5
A. F. C.	24	69 22	179.4	2.076	1.792	33.7	—3	39.1	— 2
Emma W.*...	26	57.32	164.8	1.831	1.642	29.9	—8	33.3	—10
Average for men..........						34.7	...	39.7	
Average for women..........						32.3	...	37.0	

* Unusually quiet subjects.

TABLE 3.—THE BASAL METABOLISM DETERMINATION OF AVERAGE NORMAL FOR MEN BETWEEN AGES OF 20 AND 50*

Name	Details Published in Paper	Average Calories per Sq. M. per Hour, Linear Formula
G. L.	4	40.7
E. F. D. B.	4 and 11	39.4†
R. H. H.	4	40.9
L. C. M.	4	40.5
F. C. G.	4	37.7
Morris S.	7	41.2
Albert G.	11 and 13	41.2
R. H. S.	11	37.4
A. F. C.	13	39.1
Average, Sage normal controls..........		39.7
Average, Means' normal controls..........		39.6
Average, Benedict s normal controls..........		38.9

* Average calories per square meter per hour, according to the "Linear Formula," of men examined in Sage calorimeter. It has been impossible to find John L. and measure his surface area.

† Average of four basal experiments, Paper 4, first experiment Paper 11.

we add to the group the seven women studied by Means[5] the average for the whole would be 36.9 calories, a figure which may be adopted as the standard for normal women. This shows that the metabolism of women is about 7 per cent. lower than that of men, a figure in agreement with the conclusions of Benedict and Emmes.

TABLE 4.—A COMPARISON OF THE METABOLISM OF FAT AND THIN SUBJECTS TAKEN LARGELY FROM THE WORK OF BENEDICT, EMMES, ROTH AND SMITH

Name	Per Cent. Deviation from Normal Average, 34.7	39.7	Calories per Kg. per 24 Hours	Name	Per Cent. Deviation from Normal Average, 32.3	36.9	Calories per Kg. per 24 Hours
	Meeh's Formula	Height-Weight Formula			Meeh's Formula	Height-Weight Formula	
Fat Men—				Fat Women—			
W. S.	− 1.2	+ 5.0	22.8	Dr. M. D.	−11.2	− 1.0	18.9
O. F. M.	− 8.6	− 0.5	21.3	O. A.	− 9.6	0.0	19.5
Prof. C.	−15.1	−12.0	19.9	H. H.	−17.0	− 7.0	18.0
F. E. M.	− 6.9	− 4.0	22.7	H. D.	−10.3	+ 1.0	20.1
F. A. R.	− 6.1	− 8.0	22.9	F. M. R.*	− 6.8	+ 7.0	21.0
				D. L.*	−13.5	+ 1.0	19.7
				L. F. W.*	−16.9	0.0	18.6
Average	− 7.6	− 4.0	21.9	Average	−12.2	0.0	19.4
Thin Men—				Thin Women—			
R. A. C.	+11.8	− 2.0	29.7	J. T.	+12.5	+ 2.0	31.7
B. N. C.	+ 7.2	− 6.0	29.8	A. A.	+ 9.6	− 5.0	32.0
L. E. A.	+ 7.6	− 2.0	29.5	E. W.	−12.2	+ 7.0	31.5
A. F. G.	− 0.8	−10.0	27.0	A. C.	− 0.5	− 8.0	27.4
				J.	− 2.1	− 7.0	26.9
				L. B.	− 6.7	−13.0	24.9
Average	+ 6.4	− 5.0	29.0	Average	+ 4.2	− 4.0	29.1

* Means' subjects.

A COMPARISON OF FAT AND THIN SUBJECTS

In Paper 4 of this series attention was called to the fact that in the case of fat individuals Meeh's formula would give a figure for the calories per square meter which would be very much too low. It might have been added that in the case of thin subjects the figure would be very much too high. The male subjects of Benedict and co-workers were plotted in our previous paper according to height and weight, and on account of the above mentioned errors six fat men and two thin ones were excluded from the averages. Now that it is possible to correct the error in Meeh's formula it has seemed advisable to compare

the metabolism of the fat and thin groups. A table compiled by the insurance companies showing the average weight of the male applicants between the ages of 25 and 29 years for different heights was taken as a standard. Those subjects whose weight departed more than 20 per cent. from this standard were considered either fat or thin. H. F. was excluded on account of old age, two more thin men, L. E. A. and A. F. G., were included in the new list. The fat and thin women were tabulated and three stout subjects of Means[5] added to the list. The results given in Table 4 are expressed in terms of variation from the averages for all normal controls, 39.7 calories per sq. meter per hour "Linear Formula" for the men and 36.9 for the women. According to body weight the fat and thin groups show a difference of 41 per cent.; according to Meeh's formula 15 per cent., according to the "Linear Formula" 3 per cent. This shows that Rubner's law that metabolism is proportional to surface area holds for fat and thin subjects and that we can safely use our new baseline for hospital patients whether they be fat or thin.

TABLE 5.—BASAL METABOLISM OF NORMAL MEN AND WOMEN 40 TO 60 YEARS OLD, RECALCULATED IN TERMS OF SURFACE AREA BY THE "HEIGHT-WEIGHT" FORMULA

Subject	Investigators	Age, Years	Per Cent. Deviation from Average Cal. per Sq. M. per Hr. (20-50 Yrs.)
Men			Av. 39.7
A. L.	B. E. R. and S.	40	— 2.0
F. G. B.	B. E. R. and S.	41	— 8.0
Dr. P. R.	B. E. R. and S.	41	—12.0
Dr. S.	B. E. R. and S.	43	—20.0
Prof. Z.	M-L. and F.	43	— 5.0
John L.	G. and D. B.	44	—12.0
G. L.	G. and D. B.	47	+ 3.0
W.	M-L. and F.	56	— 5.0
E. J. W.	B. E. R. and S.	58	—17.0
Women			Av. 36.9
B. K.	M-L. and F.	40	+10.0
Mrs. H. D.	B. E. R. and S.	42	+ 1.0
Dr. M. D.	B. E. R. and S.	44	— 1.0
Mrs. S. O.	B. E. R. and S.	52	—12.0
Mrs. E. B.	B. E. R. and S.	53	— 1.0
Average, men and women		40 to 50	— 4.3
Average, men and women		50 to 60	—11.3

INFLUENCE OF AGE

In Table 5 are grouped the corrected results for the normal controls between 40 and 60 years of age. In Paper 4 the subjects between the ages of 20 and 50 were grouped together, but it is apparent that the average metabolism between the ages of 40 and 50 is 4.3 per cent. lower than that of the whole group, while those between 50 and 60 are 11.3 per cent. lower. It is necessary to use a lower figure for the baseline after the age of 50, and perhaps advisable to make the change at the age of 40.

VARIATIONS IN METABOLISM

We have already spoken of the extremes in the oxygen consumption of the same individual during the course of months and years as reported by Benedict. Only a few of the subjects here reported have been studied over long enough periods to give much evidence on the question. The basal metabolism of E. F. D. B. was 35.91 calories per square meter per hour on March 13, 1913, the first time he was in the calorimeter, when he was somewhat restless. In May, 1913, it was 33.29; in March, 1914, 34.09; May, 1914, 32.97; May, 1915, 32.86. The extreme range was 9 per cent., and, excluding the first experiment, 3.7 per cent. Albert G. showed a variation of 6.4 per cent., the metabolism being unusually low on December 28, when he dozed during the two-hour experiment. In Paper 7 it will be noted that the curves representing the metabolism of the typhoid patients are very uniform.

INFLUENCE OF FOOD

In a footnote to Paper 4 it was stated that Morris S. showed a rise of 6.5 per cent. in metabolism two to six hours after a meal containing 9.6 gm. nitrogen. On recalculation the rise during the period turns out to be 7.4 per cent., and if we exclude the third period when he slept forty minutes, 11.9 per cent. This corresponds with the rise of 12 per cent. found in the case of E. F. D. B. after a similar meal containing 10.5 gm. nitrogen. Albert G. on January 6, one to four hours after 115 gm. of commercial glucose, the equivalent of 100 gm. dextrose, showed an average metabolism 11 per cent. higher than the basal determination two days later. This corresponds with the average of 9 per cent. obtained with G. L. and E. F. D. B. in the previous investigation. The one experiment on Albert G. one to five hours after 79 gm. olive oil showed little increase in metabolism. Fat exerts its chief specific dynamic action in the period immediately succeeding the hours studied. The glucose experiment on Albert G. January 4 was too short to be of value.

The average metabolism of fat and thin subjects is the same according to surface area when the surface area is correctly measured. The metabolism of women averages 37.0 calories, or 6.8 per cent. lower than that of men. A group of men and women between the ages of 40 and 50 gave figures 4.3 per cent. below, and a group 50 to 60 years old 11.3 per cent. below the average for the larger group between the ages of 20 and 50.

Under the atmospheric conditions of the calorimeter experiments the average water elimination by normal men through skin and lungs is 28.4 gm. an hour. About 24 per cent. of the heat produced is dissipated in the vaporization of water.

The figures for the specific dynamic action of protein and glucose previously obtained are confirmed. A table of normal standards is given.

CLINICAL CALORIMETRY

FOURTEENTH PAPER

METABOLISM IN EXOPHTHALMIC GOITER*

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To those who are accustomed to think in terms of the energy requirement, exophthalmic goiter stands out *par excellence* as the disease of increased metabolism, and the increased metabolism stands out as the chief symptom of hyperthyroidism. The determination of the heat production seems to afford the best index of the severity and course of the disease. There is great need of some purely objective test in hyperthyroidism to indicate the effect of treatment, since psychotherapy can modify profoundly all subjective symptoms. At present the scientific status of the treatment of exophthalmic goiter is about at the point where we would be with diabetes if there were no laboratory tests for glucose and the acetone bodies.

No one of the simpler objective tests taken alone gives an accurate idea of the course of the disease; but when a number are taken together and added to the clinical impression of the observer, they afford a rough measure of the severity of the case. The rapidity of the heart action is perhaps the best guide, but the heart is often affected by other conditions, and damage to the heart may outlast the other symptoms. Rise in temperature is so irregular as to preclude its use as a reliable

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* From the Russell Sage Institute of Pathology, in Affiliation with the Second Medical Division of Bellevue Hospital.

index. Changes in the size of the gland do not parallel the course of the disease. Changes in weight, warmth of skin and sweating are but consequences of the increase in heat production. Eye symptoms, tremor, nervous irritability, weakness, diarrhea are all too variable to be of reliance and are too difficult to measure accurately. The blood pressure is of some use as a guide, but it is affected by age and the condition of the cardiovascular system. The sugar tolerance depends on other ductless glands as well as the thyroid, and even in health has wide limits. The mononucleosis which has been considered characteristic by Kocher, Halsted and others is found in other diseases, and does not seem significant enough to be our main reliance.

In contrast to the above mentioned symptoms, an increased basal metabolism is found with great regularity in exophthalmic goiter, and in severe cases reaches a level found in no other condition. On the other hand, in cretinism and myxedema the metabolism is lower than in any other disease. The administration of thyroid extract, particularly in myxedema, raises the heat production. All other diseases in which metabolism is increased are easily distinguishable from exophthalmic goiter, and they never approach the extremes found in this condition. The basal metabolism is higher than normal in youth, in fever, in lymphatic leukemia and pernicious anemia, in severe cardiac disease, and in some cases of severe diabetes and cancer. It is lower than normal in old age, in some wasting diseases and perhaps in some cases of obesity. Diseases of the ductless glands other than thyroid show in some cases an increase, in some a decrease; but these are comparatively small.

The theories of exophthalmic goiter at present are in a somewhat chaotic state. The suprarenals, thymus and most of the other ductless glands are thought by many to be involved, and the symptoms have lately been divided into sympatheticotonic and vagotonic groups. Even in regard to the thyroid itself some advance the theory of dysthyroidism in addition to or in place of hyperthyroidism. Such confusion is natural when we have few objective tests and many bizarre symptoms which can be ascribed at will to various ductless glands whose functions are obscure. It would seem as if we needed more laboratory work for those who hold no brief for any particular kind of therapy. Even the most extreme advocates of the new theories ascribe the chief rôle to an overactivity of the thyroid gland. For the purpose of simplicity in this paper one may consider the symptoms of exophthalmic goiter to be caused by too much thyroid secretion, and allow the reader to select for himself those cases in which he believes other glands to be involved.

PREVIOUS STUDIES OF THE RESPIRATORY EXCHANGES

The question of the metabolism in exophthalmic goiter has been reviewed by Magnus-Levy,[1] Hirsch,[2], and Falta;[3] Scholz[4] has given a large number of references on the subject of cretinism.

Friedrich Müller,[5] in 1893, first pointed out the increase in metabolism in exophthalmic goiter by showing that a patient lost weight and nitrogenous substances on a diet that was more than sufficient to cover the needs of a normal person. Magnus-Levy[6] two years later was the first to demonstrate the increase in the respiratory metabolism in hyperthyroidism and the decrease in myxedema. Since then he has studied many cases of both diseases and has used the respiratory metabolism as an index of the effects of treatment, thus demonstrating the increase in heat production following the administration of thyroid extract. He found that in myxedema the rise in heat production began in the first week of the administration of the extract and increased gradually till the fourth or fifth week. The effect was most pronounced in severe cases, causing a rise of from 50 to 70 per cent. In the mild cases the increase was slight, never going above 20 per cent., and in five of the nine normal controls there was no rise at all. Stüve,[7] who worked with Magnus-Levy, found that thymus extract had no effect on the heat production. Magnus-Levy and Stüve found the metabolism greatly increased in exophthalmic goiter, and their results, together with those of the others who have studied this subject, are recorded in Table 1. Thiele and Nehring,[8] and Anderson and Bergman[9] studied the influence of thyroid extract, the former finding an increase in the metabolism of obesity patients after its use and the latter no increase with two normal men.

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1. Magnus-Levy: Von Noorden's Handbuch der Pathologie des Stoffwechsels, Berlin, 1906.
2. Hirsch, Rahel: Oppenheimer's Handbuch der Biochemie, iv, 2, 165.
3. Falta: Die Erkrankungen der Blutdrüsen, Berlin, 1913.
4. Sholz: Klinische und Anatomische. Untersuchungen über den Cretinismus, Berlin, 1906.
5. Müller, Friedrich: Beiträge zur Kenntniss der Basedowische Krankheit, Deutsch. Arch. f. klin. Med., 1893, li, 335.
6. Magnus-Levy: Gaswechsel bei Thyroidea, Berl. klin. Wchnschr., 1895, xxxii, 650; Untersuchungen zur Schilddrüsenfrage, Ztschr. f. klin. Med., 1897, xxxiii, 269; Ueber Myxoedem, ibid, 1904, lii, 201.
7. Stüve: Respiratorische Gaswechsel bei Schilddrüsenfutterung Morbus Basedowii u. s.w., Fest. Stadt. Krankenh., Frankfurt a. M., Mahlau, 1896.
8. Thiele and Nehring: Untersuchungen des respiratorischen Gaswechsel unter dem Einflusse von Thyreoideapraparaten und bei anaemischen Zustanden des menschen, Ztschr. f. klin. Med., xxx, 41.
9. Anderson and Bergmann: Einfluss der Schilddrüsenfutterung auf den Stoffwechsel des gesunden Menschen, Skand. Arch. f. Physiol., 1898, viii, 326.

TABLE 1.—GOITER CASES IN THE LITERATURE ARRANGED—

Observer	Patient	Sex*	Age, Years	Duration of Disease, Years	Clinical Classification
Hirschlaff	Louise B.	♀	..	9	Very severe last ten days of life
Author	Case 6 (Anna K.)	♀	26	10	Severe
Author	Case 3 (James McE.)	♂	29	9(?) ½(?)	Severe
					100% above average for women
Salomon	R. H.	♂	40	11	Five months before death
Hirschlaff	Louise B.	♀	21	9	Severe first two months in hospital
Magnus-Levy	Frl. E. B.	♀	20	..	Severe; acute
Salomon	Fall I	♂	23	5	
Magnus-Levy	Fr. Kr.	..	26	26	Very severe; pregnant six months
Undeutsch	Ja.	♀	24	½	"Ziemlich Schwer"
Author	Case 1 (Max W.)	♂	40	1½	Severe
Magnus-Levy	Hr. G.	♂	25	..	Severe
Undeutsch	K.	♀	23	4	(Mod. severe?)
Magnus-Levy	Frau Schr.	♀	42	..	Very severe
Pribram and Porges	E. Tesch.	♀	23	2	(Mod. severe?)
Author	Case 2 (Edwin T.)	♂	20	½	Acute; mod. severe
Pribram and Porges	M. S.	..	25	½	(Acute; mod. severe ?)
Salomon	M. J.	♀	25	1½	(Mod. severe?)
Magnus-Levy	Frl. E. T.	♀	22	..	Severe
Magnus-Levy and Stüve	Fr. R. B.	♀	26	..	Severe
Author	Case 4 (Dr. G. S. L.)	♂	52	3 - 4	Severe
Salomon	Fall II	♀	19	½	
					50% above average for women
Magnus-Levy	Hr. J.	♂	20	..	Severe
Falta	J. H.	..	22	..	(Mild?)
Falta	R. Fl.	♀	3½	3	(Severe?)
Author	Case 9 (Marion B.)	♀	22	3	Mild; operated
Author	Case 8 (Sarah M.)	♀	29	8	Mild; operated
Magnus-Levy	Frl. Ung.	♀	55	..	Severe
Author	Case 7 (Anna R.)	♀	29	5	Moderately severe
Author	Case 10 (Margaret L.)	♀	51	1	Atypical cardiac
Magnus-Levy	M. P.	♂	11½	..	Small struma, otherwise normal
Magnus-Levy	Fr. O.	♀	54	..	Simple goiter
Stüve and Magnus-Levy	Frl. G. W.	♀	24	..	Severe

—According to the Level of the Respiratory Metabolism

Calories per Sq. M. per Hr. Meeh	Pulse Rate	Blood Pressure, Syst.	Enlargement of Heart to Left, Cm.	Enlargement of Thyroid	Exophthalmos	Von Graefe Sign	Mental Irritability	Tremor	Warmth of Skin	Emaciation	Remarks
72.1											
66.1	122	.....	0	+	+	±	++	+	++	+	After ligation of 2 arteries
65.6	100-124	130-146	3.5	++	+	+	++	+	++	++	Alcoholic
64.6											
61.7	110-120	.....	0	+	—	—	+	....	.....	++	
61.7	100-130	.....	±	+	++	++	++	+	++	+	
60.0	120										
58.0	++	.....	+	+	++	++	+	+	+	++	
57.2	142										
56.6	++	.....	+	+	+	—	++	++	+	+	
55.4	100-136	130-150	2.5	++	++	±	+++	+	++	±	
54.4	112										
53.7	92-122	.....	+	+	++	....	....	+			
53.1	130-150										
53.0	++	.....	+	..	....	....	+	+			
50.6	92-112	140-150	0	+	+	±	++	+	++	±	
50.2	++	.....	+	+	+	+	....	+			
49.7	90-100	.....	±	+	—	—	+	+	+	±	
49.6	100										
49.3											
49.2	97-101	148	2	++	+	+	+	++	++	+	After ligation of 4 arteries
48.7	90-124	.....	+	+	+	+	....	....	.....	±	
48.5											
46.1	122										
44.8	.....	.....	..	..	—	—	....	+	+		
44.5	80-150	130	..	+	+	++	++	+	++		
44.1	.....	.....	..	..	+	....	+	....	+	—	Par. thyroidect. 2 and 1 yrs. ago
43.8	.....	.....	0	+	—	—	+	+	±	....	Partial thyroidectomy 8 yrs. ago
43.5	120										
43.4	84-92	.....	0	+	+	+	+	+	+	+	
42.0	68-88 Fibril	170	2-3	++	+	+	+	....	++	+	
40.6	.....	.....	—	±	—	—	....	—	.....	—	
40.6	94										
39.9	100-120										

TABLE 1.—

Observer	Patient	Sex*	Age, Years	Duration of Disease, Years	Clinical Classification
Magnus-Levy........	Frl. M. Kr.	♀	20	..	Mild ....
Falta................	Ad. K.	♂	33	6	(Severe?) ....
Undeutsch...........	Wit.	♀	24	14?	"Forme fruste" ....
Magnus-Levy........	Hr. Be.	♂	20	..	Mild ....
Magnus-Levy........	Frl. E. W.	♀	21	..	Severe ....
Magnus-Levy........	Fr. B.	♀	52	..	Half way between Kropf and forme fruste
Author...............	Case 5 (Peter N.)........	♂	28	5	Atypical; operated ....
					Upper normal limit for women......
Magnus-Levy........	Hr. R. B.	♂	20	..	Mild ....
					Average for normal men............
Magnus-Levy........	Frl. U.	♀	55	..	Typical; mild ....
Author.........	Case 11 (Miss B. H.).....	♀	31	4	Atypical; operated ....
Magnus-Levy.	Frl. E. D.	♀	25	..	Simple goiter ....
Magnus-Levy........	Frl. Sch. M.	♀	28	..	Mild ....
Magnus-Levy........	Frl. M. Kl.	♀	17	..	Simple goiter ....
					Average for normal women.........
Magnus-Levy........	Frl. Rh.	♀	36	..	Half way between Kropf and forme fruste; simple goiter

* In this column, ♂ denotes male and ♀ female.

Hirschlaff[10] made one of the most valuable contributions to the subject by studying in great detail over a long period a very severe case of hyperthyroidism which eventually came to necropsy. The oxygen consumption of this patient was about 77 per cent. above normal, rising to 105 per cent. above normal in the last week of life. Magnus-Levy considers that some of the high results on this patient were due to restlessness, but some were obtained while she was under the influence of morphin. This careful laboratory work on one patient is of more value to science than the clinical observation of a hundred patients. Jaquet and Svenson[11] found no constant rise in metabolism when they treated cases of obesity with thyroid extract. They also studied the specific dynamic action of food on these patients, and concluded that it was less than normal before treatment with thyroid

10. Hirschlaff, W.: Zur Pathologie und Klinik der Morbus Basedowii, Ztschr. f. klin. Med., 1899, xxxvi, 200.

11. Jaquet and Svenson: Zur Kentniss des Stoffwechsel fettsuchtigen Individuen, Ztschr. f. klin. Med., 1900, xli, 375.

—(*Continued*)

Calories per Sq. M. per Hr. Meeh	Pulse Rate	Blood Pressure, Syst.	Enlargement of Heart to Left, Cm.	Enlargement of Thyroid	Exophthalmos	Von Graefe Sign	Mental Irritability	Tremor	Warmth of Skin	Emaciation	Remarks
39.7	80										
39.7	120-140	140	2	++	−	−	+	++	++	+	
37.7	100+	125	0	+	−	−	++	++	+	±	
37.0	78										
36.5	128										
35.7	96	.....	±	+	−	−	....	±			
35.5	72-94	.....	1	±	−	−	+	++	−	+	Four arteries ligated 1 yr. ago
35.5											
34.7											
34.7											
34.7	58-90										
34.6	72-96	112-120	0	−	±	−	++	+	−	+	Par. thyroidect. 2 mos. ago
34.6	86										
34.1	80										
3.30											
32.3											
29.4	72-92	.....	0	±	±	+	....	±	.....	....	Hysterical temperament

extract but greater than normal after treatment. Salomon[12] considered the increase in metabolism to be the most important objective symptom of hyperthyroidism, and followed it during treatment with "Radogen" and the serum of a thyroidectomized horse. Neither of the remedies caused a fall in the metabolism. Steyrer[13] studied the effects of thyroid tablets on one exophthalmic goiter and one myxedema patient, using a Pettenkofer-Voit respiration chamber. Pribram and Porges,[14] working under Salomon, studied the "nüchtern" or basal metabolism from fifteen to seventeen hours after the last meal of diets containing various amounts of nitrogen. They found the heat production from 4 to 8 per cent higher the morning after a diet containing from 31 to 42

12. Salomon, H.: Gaswechseluntersuchungen bei Morbus Basedowii und Akromegalie, Berl. klin. Wchnschr., 1904, xxiv, 635.

13. Steyrer, A.: Ueber die Stoff und Energieumsatz bei Fieber, Myxoedem und Morbus Basedowii, Ztschr. f. exper. Path. u. Therap., 1907, iv, 720.

14. Pribram and Porges: Ueber den Einfluss verschiedenartiger Diätformen auf den Grundumsatz bei Morbus Basedowii, Wien. klin. Wchnschr., 1908, xxi, 1584.

gm. of nitrogen than after mixed diets rich in carbohydrate. They do not consider that this differs from what would be found in normal persons after such excessive protein feeding, and believe that the basal metabolism is not much influenced by protein or meal abstinence. In one patient two treatments with the Roentgen ray did not cause any drop in the oxidative processes. More recently Undeutsch,[15] using the Rolly-Rosiewicz modification of the Benedict universal respiration apparatus, compared the rise in metabolism following the administration of various forms of protein to patients with exophthalmic goiter. He found that 40 gm. of Aleuronat increased the metabolism more than 35 gm. Roborat, and that both had greater action than 200 gm. chopped beef. Two normal controls gave the same results. He concludes that animal protein has a lower specific dynamic action than vegetable. Undeutsch also made observations on three of his patients from one to two weeks after a partial thyroidectomy. One patient showed a drop of more than 10 per cent. in the heat production, one a drop of 20 per cent. and a third with "forme fruste" and colloid goiter only a slight reduction.

Von Bergman[16] studied several myxedema patients, finding the metabolism moderately decreased. He observed a rise of 25 per cent. in the heat production in an obesity patient after the administration of thyroid extract. Falta[8] reports respiration experiments on three of his exophthalmic goiter patients made by Dr. Bernstein. Means,[17] studying several obesity patients and making a large number of respiration experiments on one marked case, found a marked rise in metabolism after thyroid administration.

The literature on the treatment of exophthalmic goiter is too enormous to be reviewed in this paper, and only those remedial measures used on the patients here described will be discussed. A partial thyroidectomy has been and perhaps always will be the standard method of treatment. Recently many surgeons have been ligating one or more of the thyroid arteries under local anesthesia as a preliminary to the more radical operation or in place of it. Medical treatment gives slower results which are often very satisfactory. Mental and physical rest over long periods of time, combined with abundant food, almost invariably improves the patient's condition, and in many cases there is a tendency toward recovery without any treatment. Beebe and

15. Undeutsch, W.: Experimentelle Gaswechseluntersuchungen bei Morbus Basedowii; Grundumsatz und Umsatz nach Aufnahme von animalischem und vegetabilischem Eiweiss, Inaug. Dessert., Leipzig, 1913.

16. Von Bergman: Der Stoff und Energieumsatz beim infantilem Myxoedem und beim Adipositas universalis mit einem Beitrage zur Schilddrüsenwirkung, Ztschr. f. exper. Path. u. Therap., 1909, v, 646.

17. Means: Studies of the Basal Metabolism in Obesity and Pituitary Disease, Jour. Med. Research, 1915, xxxii (New Series, xxvii), 121.

Rogers,[18] and more recently Beebe[19] alone, have used a cytotoxic serum prepared by injecting sheep with an extract of human thyroid tissue. This serum has never come into general use. Some patients cannot take the serum on account of violent local and constitutional reactions, and others who can take it show little improvement, as is the case with all other forms of treatment. Rogers[20] uses partial thyroidectomy in some cases, and serum in a few others, but places his chief reliance on ligation of two or more of the thyroid arteries as giving the best results in the long run. He has used thyroid extract in some cases for a few days after the ligation, and in other asthenic patients has given a thyroid preparation called "X Thyroidin," or thyroid "residue." Forcheimer[21] is very enthusiastic about the quinin-ergotin treatment which he devised several years ago. He gives quinin hydrobromate, 5 grains, and ergotin, 1 grain in gelatin coated pills four times a day. All of the foregoing clinicians insist on rest from work and mental relaxation as part of the treatment.

Plummer[22] has recently abstracted the histories of the unusually large number of cases treated at the Mayo Clinic, and on the basis of averages has arranged the symptoms in the order of their onset as follows: (1) cerebral stimulation; (2) vasomotor disturbances of the skin; (3) tremor; (4) mental irritability; (5) tachycardia; (6) loss of strength; (7) cardiac insufficiency; (8) exophthalmos; (9) diarrhea; (10) vomiting; (11) mental depression; (12) jaundice; (13) death. Of especial interest is the work of Rudinger[23] on the nitrogen minimum in hyperthyroidism. He places his patients on Landergren's low nitrogen diet, and found the nitrogen output to be so much greater than in normal persons that he considers there is a 100 per cent. increase in the destruction of body nitrogen on the fourth day of the diet. In regard to the discussion as to whether we are dealing with a hypersecretion or abnormal secretion of the thyroid, it may be well to call attention to the statement of Magnus-Levy, "The quantitative relations

18. Rogers, John, and Beebe, S. P.: The Treatment of Hyperthyroidism by a Specific Cytotoxic Serum, The Archives Int. Med., 1908, ii, 297.

19. Beebe, S. P.: The Serum Treatment of Hyperthyroidism, Jour. Am. Med. Assn., 1915, lxiv, 413.

20. Rogers, John: The Course of Acquired Disease of the Thyroid Gland and the Principles which Seem to Control Its Progress, Ann. Surg., 1914, p. 281; Exophthalmic Goiter and Its Treatment, New York State Jour. Med., 1915, xv. 4; Am. Jour. Physiol, 1915, xxxvi, 113; ibid., 1915, xxxvii, 121, 453; ibrid., 1915, xxxix, 154; ibid., 1916, xxxix, 345.

21. Forcheimer, F.: Exophthalmic Goiter, in Therapeusis of Internal Diseases, 1913, iii, 895.

22. Plummer, H. S.: The Clinical and Pathologic Relationships of Hyperplastic and Nonhyperplastic Goiter, Jour. Am. Med. Assn., 1913, lxi, 650.

23. Rudinger: Ueber den Eiweissumsatz bei Morbus Basedowii, Wien. klin. Wchnschr., 1908, xxi, 1581.

of thyroid secretion are almost totally unknown, and are much too complicated to allow our following out a theory of hyperthyreosis in all its details; much less . . . does it enable us to argue a theory of dysthyreosis." Falta, Newburgh and Nobel,[24] on the basis of experiments with various organ extracts, believe in "Ueberfunction" rather than "Dysfunction" in exophthalmic goiter, and consider that the difference in symptoms is due to differences in the constitution of the patient.

METHODS OF EXPERIMENT

Most of the patients studied over considerable periods of time remained in the metabolism ward described in Paper 3 of this series. They were placed in the respiration calorimeter in the morning hours, either without breakfast or after special meals, if the tests were being made to determine the specific dynamic action of food. Each patient was put in the calorimeter for half an hour or so a day or two before the first experiment, in order to let him become accustomed to the interior of the apparatus. No patient objected, since all realized that their treatment was being controlled by the results of the observations. Some of the patients had marked tremors when they moved, but inside the calorimeter they were lying quietly on a comfortable bed, and they moved but seldom. The work-adder was of great service in giving an accurate idea of the relative activity of the subject in each period. In the severe cases with moist skin, the work-adder was even more sensitive than usual, since any movement on the part of the patient liberated an abnormal amount of moisture from the bedding and clothing, expanding the air of the box to a marked degree. This accounts for some of the high readings of this instrument; but some of the patients with severe cases were distinctly restless, particularly toward the end of an observation. It was for this reason that short experiments were used by preference.

The female patients were taken directly from the general medical or surgical wards. A few of both sexes came to the calorimeter room from their homes in the neighborhood, lying down for at least two hours before the observation began. Great care was taken to avoid fatigue or excitement, since it was apparent that the metabolism of these thyroid patients showed great lability.

CASE HISTORIES

CASE 1.—*History.*—Max W., aged 40, storekeeper, born in Roumania, Hebrew, admitted Feb. 11, 1914. Had typhoid fever when 18 years old. Two years ago he was operated on for inguinal hernia. About this time he was refused life insurance because he weighed 190 pounds. He drinks little, but smokes from fifteen to twenty cigarets a day.

24. Falta, Newburgh and Nobel: Ztschr. f. klin. Med., 1911, p. 72.

Present Illness.—In January, 1913, he received news of the violent death of his brother, and was much excited for a week. The next month he suffered from a severe unproductive cough, was nervous and lost weight. He was sent to the mountains with a diagnosis of tuberculosis, but did not improve. The Wassermann reaction was found to be strongly positive, and he was treated with mercury, still without improvement. October 13, he went to Mount Sinai Hospital, where a diagnosis of exophthalmic goiter was made and medical treatment tried. Shortly afterward he went to the Presbyterian Hospital, where his protein and carbohydrate metabolism was studied by Dr. Geyelin.[25] It was found that the blood sugar was 109 mg. per hundred c.c., the phenolsulphonephthalein output 85 per cent., the leukocytes 11,250, polymorphonuclears 68 per cent., lymphocytes 24 per cent., large mononuclears 5 per cent., and eosinophils 3 per cent. The urine showed traces of sugar, and the Wassermann test was strongly positive.

Physical Examination.—Feb. 11, 1914, the patient is 173.7 cm. tall, of rather large frame with small hands and tapering fingers. The skin is dark, flushed, warm and slightly cyanotic. The beard is thick, the pubic hair normal but the hair on the chest scant and the breasts fatter than the rest of the body. The face is broad and flat, the expression angry and the eyes staring with slight protrusion. The upper lid covers about 2 mm. of the cornea, but does not follow the cornea when the patient looks down. There is some weakness of convergence; he winks but seldom, and the forehead wrinkles but slightly.

There is moderate soft enlargement of the thyroid, especially the right lobe. The neck measures 37 cm. in circumference. The apex of the heart is in the fifth space 11 cm. to the left of the midline, and the limit of dulness 12.5 cm. to the left. The action is rapid and shows a marked irregularity, apparently respiratory in type, with long pauses at the end of expiration. There is a soft systolic murmur at the apex. Carotid pulse is large, radial small. The hands show red areas on the thenar and hypothenar eminences, and there is a tremor when he is excited. There is a scar of an old left inguinal hernia operation, and the left testis is very small and soft; the right testis is large, but of normal consistency. His disposition is nervous, he is excitable, quick in thought and action, and he takes malicious pleasure in teasing his fellow patients, a cretin and a pituitary patient, both somewhat slow mentally.

Treatment and Course.—The data concerning the food and urine are given in Table 2. In February and March the temperature was between 98.4 and 100, the pulse 110-140, the respirations from 26 to 28. March 18, the patient had an acute follicular tonsillitis with a transient rise in temperature to 103.2. Two days later it was normal. During April the temperature was below 99.6, the pulse 104-124, respirations from 20 to 22. Blood pressure, February 15, systolic, 150, diastolic, 70; March 7, 130-60; April 6, 132-82; April 23, 148-74. Beebe's serum was begun, March 5, and the doses slightly increased from time to time. The patient received twenty-three doses up to April 30, and after this the serum was given by Dr. Beebe, himself, at fairly regular intervals. With the serum he was given 1 grain of potassium iodid twice a day. The local reaction from the injection was at times quite marked, but the patient felt so much better that he cheerfully submitted to the discomfort and was enthusiastic about the treatment.

During his stay in the hospital he averaged about three stools a day. He improved distinctly even before he received any treatment other than rest in bed and good food. The diarrhea stopped, as did the sweating, and he was not so nervous. There was slight glycosuria after 100 gm. of glucose. A note, April 15, says he weighed more than on admission, that he was eating more and was feeling stronger each day. It was noticed that he had a polyuria,

25. Geyelin, H. R.: The Carbohydrate Metabolism in Hyperthyroidism as Determined by Examination of Blood and Urine, The Archives Int. Med., 1915, xvi, 975.

TABLE 2.—Clinical Data in Case 1

Date	Temperature		Total Calories Food	Carb., Gm.	Fat, Gm.	Food N.	Urine N.	Body Weight	Urine, Volume, c.c.
	Max.	Min.							
2/13/14	99.6	98.6	2,974	176.0	179.0	15.7	14.88	.....	2,785
2/14/14	99.6	98.6	3,675	232.0	234.0	21.3	13.87	62.24	2,500
2/15/14	99.6	98.6	4,091	256.0	252.0	21.5	14.58	62.00	2,450
2/16/14	99.4	98.2	3,662	230.0	238.0	19.7	12.69	61.76	2,525
2/17/14	99.0	98.6	4,324	289.0	273.0	23.3	18.15	61.89	3,150
2/18/14	100.0	98.6	3,971	313.0	228.0	18.0	15.75	62.02	3,720
2/19/14	99.6	98.6	3,970	273.0	259.0	21.8	19.25	61.81	2,720
2/20/14	99.6	98.6	3,620	299.0	201.0	20.0	17.17	61.60	3,240
2/21/14	99.0	98.6	3,801	367.0	198.0	17.6	15.58	62.26	3,045
2/22/14	99.8	98.8	3,758	289.0	216.0	21.6	18.16	62.27	3,330
2/23/14	99.6	99.0	3,874	292.0	226.0	22.6	16.19	62.28	3,240
2/24/14	99.6	99.0	3,628	274.0	212.0	21.0	17.46	61.77	3,200
2/25/14	99.8	99.2	2,411	187.0	119.0	20.9	19.91	61.17	2,890
2/26/14	99.4	98.6	4,246	310.0	282.0	22.7	17.78	61.08	2,360
2/77/14	100.0	98.6	2,583	263.0	121.0	18.0	17.36	60.90	2,990
2/28/14	99.3	98.4	3,520	271.0	205.0	19.3	14.37	60.71	2,610
3/ 1/14	99.2	98.8	3,399	284.0	184.9	20.0	15.60	60.71	3,320
3/ 2/14	99.6	98.4	2,809	199.0	157.0	20.0	18.21*	60.52	3,240
3/ 3/14	99.8	98.6	3,739	290.0	215.0	21.4	18.21*	60.29	3,150
4/ 4/14	99.8	99.0	2,842	211.0	169.0	15.7	14.59*	60.06	2,375
3/ 5/14	99.8	98.6	3,396	255.0	199.0	19.6	17.15*	60.10	2,930
3/ 6/14	99.6	99.0	3,796	273.0	207.0	20.2	12.61*	60.10	2,000
3/ 7/14	99.8	98.8	.....	.....	.....	....	.....	60.14	.....
3/22/14	99.0	98.0	.....	.....	.....	....	.....	.....	.....
3/23/14	99.4	98.8	2,328	193.0	121.0	16.0	12.16	59.25	3,136
3/24/14	99.0	98.2	3,366	252.0	198.0	19.2	10.59	.....	1.940
3/25/14	99.2	98.4	3,475	301.1	187.0	19.5	11.39	.....	3,200
3/26/14	98.4	98.4	3,408	264.0	196.0	19.6	11.27	60.01	2,890
3/27/14	99.2	98.0	3,494	305.0	187.0	19.1	11.10	60.06	2,490
3/28/14	98.4	98.4	3,640	294.0	206.0	20.0	12.36	60.12	2,960
3/29/14	98.8	98.2	3,891	333.0	214.0	20.9	11.54	60.56	3,365
3/30/14	98.8	98.4	3,560	368.0	164.0	20.4	11.32	61.00	3,460
3/31/14	99.2	98.6	3,976	398.0	195.0	21.5	13.04	61.18	2,500
4/ 1/14	99.6	98.6	4,294	437.0	213.0	20.2	12.11	61.37	2,390
4/ 2/14	98.6	98.0	4,216	422.0	212.0	20.0	12.19	61.88	2,600
4/ 3/14	98.8	98.6	4,232	419.0	215.0	20.2	11.60	61.88	2,900
4/ 4/14	99.6	98.4	4,205	405.0	217.0	20.6	11.85	61.91	2,320
4/ 5/14	99.4	98.4	4,444	435.0	225.0	21.8	12.53	62.26	2,970

* Average feces N. per day March 2 to 6, 3.67 gm.

TABLE 2.—(*Continued*)

Date	Temperature		Total Calories	Carb., Gm.	Fat, Gm.	Food N.	Urine, N.	Body Weight	Urine, Volume, c.c.
	Max.	Min.							
4/ 6/14	99.2	98.4	3,316	379.0	144.0	16.3	13.10	62.26	2,790
4/ 7/14	98.4	98.4	4,529	425.0	214.0	20.3	13.09	62.26	3,060
4/ 8/14	99.0	98.4	4,506	433.0	237.0	20.0	12.62	62.62	2,660
4/ 9/14	98.8	98.4	4,345	444.0	214.0	20.7	12.17	62.90	3,190
4/10/14	98.8	98.4	4,538	424.0	242.0	20.2	13.17	63.19	3,200
4/11/14	99.6	98.2	4,062	372.0	216.0	20.0	13.28	63.32	2,500
4/12/14	99.8	98.2	4,568	401.0	253.0	21.6	11.85	63.45	2,330
4/13/14	98.8	98.6	4,801	550.0	213.0	22.0	17.54	63.01	3,770
4/14/14	98.4	98.4	4,108	408.0	218.0	20.9	12.55	62.58	1,420
4/15/14	98.4	98.4	4,232	406.0	219.0	20.6	15.58	62.92	1,390
4/16/14	99.6	98.4	4,186	388.0	217.0	20.0	15.64	63.26	1,500
4/17/14	99.6	98.8	4.164	343.0	241.0	20.1	15.02	63.58	1,330
4/18/14	99.2	98.4	4,319	355.0	249.0	21.1	15.36	63.58	1,660
4/19/14	99.4	98.8	4,106	380.0	217.0	20.8	14.85	63.58	1,580
4/20/14	99.0	98.8	3,961	350.0	217.0	20.6	15.69	63.90	1,860
4/21/14	99.2	98.4	3,817	319.0	214.0	20.2	14.18	63.81	1,600
4/22/14	99.6	98.6	4,041	369.0	214.0	20.8	17.23	63.73	1,800
4/23/14	98.8	98.4	4,353	399.0	230.0	22.6	17.85	.....	1,960
4/24/14	98.6	98.0	2,943	280.0	151.0	15.1	14.27	63.29	1,889
4/25/14	99.0	98.6	4,064	375.0	214.0	20.7	14.40	.....	1,620
4/26/14	99.4	98.2	4,071	369.0	217.0	20.9	15.52	.....	1,840
4/27/14	99.2	98.2	4,107	361.0	215.0	20.9	15.19	64.56	1,850
4/28/14	98.8	98.2	3,997	360.0	214.0	20.6	14.55	.....	2,360

and the salt in the diet was cut down to from 3 to 4 gm. a day. Two days after this change the urine volume rose to 3,900 c.c., with 22 gm. sodium chlorid in twenty-four hours. After this the volume dropped markedly. By April 24 he was able to be up and about most of the day without fatigue. When he left the hospital the thyroid gland and the eyes were as on admission, but the heart action was regular most of the time.

A year later, April 22, 1915, he spent another day in the metabolism ward and went into the calorimeter again. He had done very well under Dr. Beebe's treatment, gaining 22 pounds in weight. He was able to work in his store eight or ten hours a day, and a few weeks ago walked 5 miles. He seldom has palpitation, but does not try to walk upstairs. He is not so excitable as a year ago. He is able to wear a collar one size smaller than last year. He looks much fatter and stronger, but the eye symptoms are unchanged and the skin is still moist and warm. The apex of the heart is maximum in the fifth space 13.3 cm. to the left of the midline, and the action is so markedly irregular as to suggest auricular fibrillation, a diagnosis which is confirmed by the electrocardiogram.

Case 2.—*History.*—Edwin T., aged 20 years, student, admitted Feb. 24, 1915, discharged May 1. At the age of 10 had an attack of acute rheumatic fever, and since then has had many sore throats. Three years ago he worked

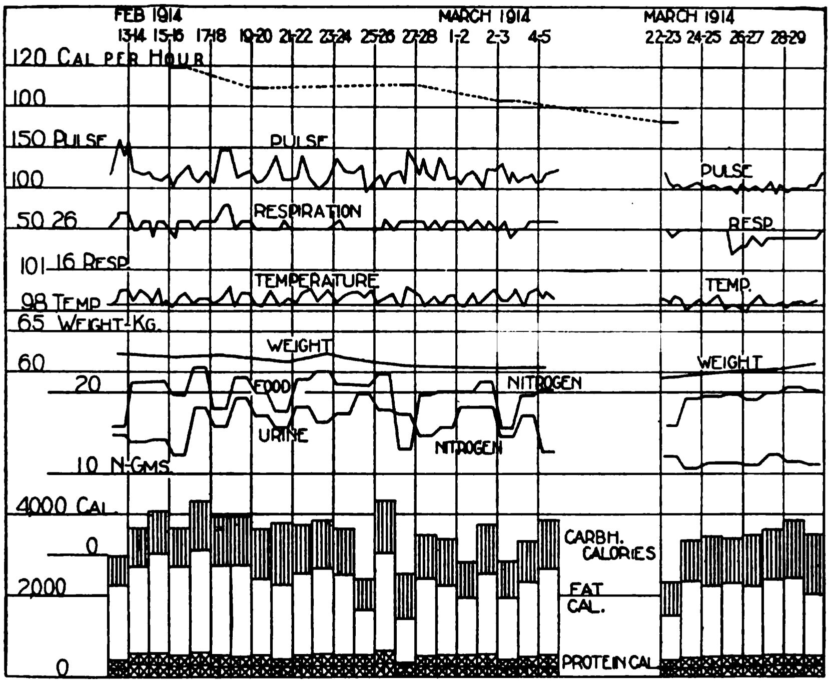

Fig. 1.—Chart in Case 1. Max W.

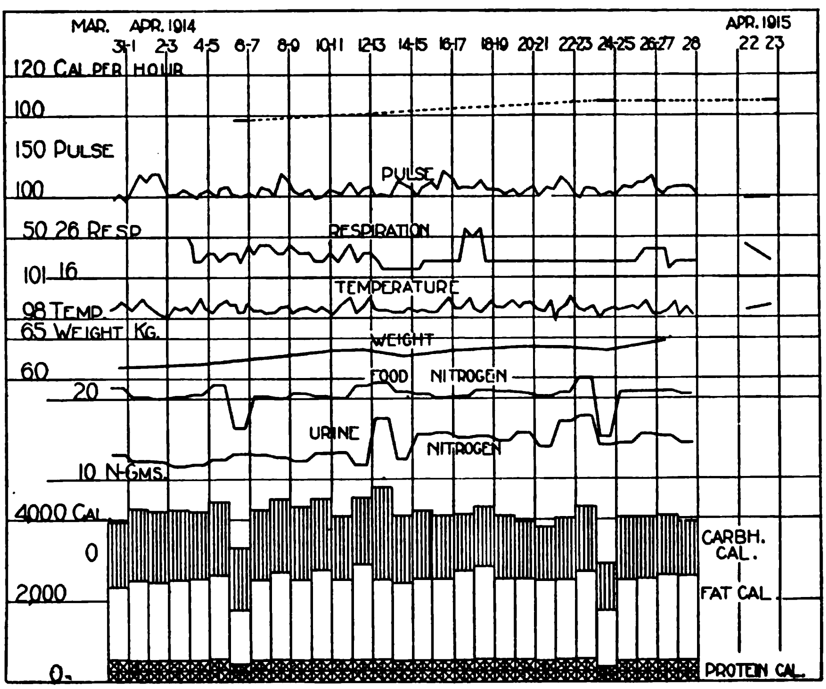

Fig. 2.—Chart in Case 1. Marx W. (continued).

very hard in school. At this time he was able to participate in track athletics. He has been accustomed to taking about six cups of strong tea every day, and has always been nervous. About six months ago he became excitable and restless and a little later was obliged to stop work. About three months ago his friends began to speak of a change in his facial expression. He grew steadily worse until three weeks ago, when a diagnosis of hyperthyroidism was made by Dr. R. J. Shea, and proper treatment started. He lost 13 pounds in weight, but regained most of it under Dr. Shea's care.

Physical Examination.—The patient is 168 cm. tall, moderately thin, the bones are slender, and the distribution of hair is normal for his age. The facies is neurotic in type and the expression angry with slight protrusio bulbi. The tonsils are large and succulent with deep crypts. The thyroid is soft and enlarged, measuring 12 cm. broad, 3 cm. in the vertical direction at the isthmus and 4 cm. at each lobe. The heart is not enlarged, but the first sound is of poor quality, short and sharp, and there is a murmur over the pulmonic area which resembles a hemic or extracardiac murmur. The heart action is forcible, but the radial pulse small. The skin is flushed, warm and moist, often breaking out into sweat. There is a tremor when he is excited.

Treatment and Course.—The first month in the hospital he was given no medication but kept quiet in bed. He became less and less excitable, the skin became cooler and drier and he was happy and helpful in the ward. About March 10 he began to be homesick and at times excitable. March 23, Beebe's serum was started in 5 minim doses almost every day. March 29, there was a severe local reaction accompanied by nausea. After this the serum was given in smaller doses every three days until April 14.

The patient felt a little better after the first few doses of serum, but later grew steadily worse, becoming more depressed, discouraged and at times very nervous. Between April 7 and 21 he was much excited over some personal matters, and was hard to manage. April 21, he was removed to the surgical ward, and the right inferior thyroid artery tied under novocain anesthesia by Dr. Rogers. April 23 and 29, the other three arteries were tied, the patient experiencing no pain, and scarcely ever showing a pulse rate above 100. He felt better and was up and about the ward the day after each operation.

May 10, he was readmitted for a calorimeter observation after ten days in the country. He has felt better and has slept well. The wounds are healing well and his general condition seems improved, but the physical examination is much the same as when first admitted to the hospital. For clinical data see Table 3.

Case 3.—*History.*—James McE., aged 29, factory worker, admitted March 1, 1915, on the service of Dr. Lockwood, with the diagnosis of exophthalmic goiter and alcoholism; at the age of 22 had an attack of appendicitis. He is a heavy smoker, drinks much tea and has periodic attacks of drunkenness lasting about a week. He has been thin, nervous and in rather poor health for the last nine years, and has been very excitable for two or three years. Seven months ago he became very nervous. Five months ago he noticed swelling of the neck, palpitation and dyspnea. At this time he had severe pains in his face not relieved by the extraction of a tooth. Two weeks ago he began to have night sweats, cough, pain in the bones, hoarseness and he lost weight rapidly.

Physical Examination.—The patient is 166 cm. tall, emaciated, restless, expression staring, skin flushed, warm and sweating, pubic and axillary hair scant. Exophthalmos moderate, von Graefe's and Moebius' signs positive. The teeth show much caries and pyorrhea. There is a marked bilateral enlargement of the thyroid gland. Thorax is poorly formed, heart apex 13 cm. to left of midline, regular but markedly overacting, with a rough systolic murmur, loudest to the left of the sternum. Pulse is Corrigan in type. There is a fine tremor of fingers and tongue, and a distinct odor of acetone on the breath.

TABLE 3.—Clinical Data in Case 2

Date, 1915	Food					Urine					
	Total Calories	Protein, Gm.	Fat, Gm.	Carbohyd., Gm.	Food N	Urine N	Excreta N, Gm. †	N Balance, Gm.	Urine Glucose, Gm.	Urine Vol., c.c.	Body Weight, Kg.
Feb. 25-26	3,107	98.7	166.7	280.9	15.79	.....	.....	......	.....	.....	50.18
Feb. 26-27	2,330*	61.7	134.0	202.7	9.87	15.69	16.68	—6.81	.....	880	49.78
Feb. 27-28	2,882	92.9	139.9	292.6	14.86	16.70	18.18	—3.32	.....	990	.....
Feb. 28- 1	2,728	87.0	142.8	254.7	13.92	17.71	19.10	—5.18	.....	1,030	49.88
Mar. 1- 2	3,704*	101.0	211.6	322.4	16.16	18.44	20.05	—3.89	.....	1,040	.....
Mar. 2- 3	3,462	98.6	184.3	327.9	15.78	16.98	18.56	—2.78	.....	990	.....
Mar. 3- 4	364.1	104.6	188.6	355.6	16.73	17.50	19.17	—2.54	.....	1,065	49.78
Mar. 4- 5	3,221	93.2	172.9	279.3	14.91	16.42	17.91	—3.00	10.64	1,050	49.40
Mar. 5- 6	2,897	132.1	125.9	288.9	22.16	19.51	21.73	+0.43	14.71	1,602	50.42
Mar. 6- 7	2,768	85.5	141.1	268.3	13.68	18.15	19.52	—5.84	15.15	1,595	50.04
Mar. 7- 8	3,760	111.0	210.2	331.6	17.76	15.55	17.33	+0.43	5.31	1,065	50.37
Mar. 8- 9	2,999	155.9	172.9	183.3	24.94	21.22	23.71	+1.23	7.92	1,627	50.06
Mar. 9-10	3,517	105.8	194.6	311.2	16.92	6.87	8.56	+8.36	0	900	50.36
Mar. 10-11	2,419	69.1	124.6	238.9	11.06	13.59	14.70	—3.64	18.06	1,018	49.32
Mar. 11-12	3,549	100.1	206.8	302.5	16.01	15.18	16.78	—0.71	7.20	1.320	.....
Mar. 12-13	3,525	97.1	204.1	299.3	15.58	11.35	12.90	+2.68	7.41	1,075	50.05
Mar. 13-14	3,728	99.5	221.3	306.7	15.92	14.68	16.27	—0.35	9.54	1,160	50.18
Mar. 14-15	3,638	97.6	199.1	333.4	15.61	15.24	16.80	—1.19	7.30	1,260	50.10
Mar. 15-16	2,075	66.9	194.5	242.3	10.70	11.80	12.87	—2.17	5.57	880	50.11
Mar. 16-17	3,130	66.5	205.3	243.4	10.64	13.28	14.34	—3.70	6.37	1,170	49.76
Mar. 17-18	3,159	67.9	202.3	243.6	10.86	8.88	9.97	+0.90	4.62	800	50.01
Mar. 18-19	3,200	70.7	203.3	248.3	11.34	12.53	13.66	—2.32	9.37	1,040	.....
Mar. 19-20	3,550	69.8	218.0	301.3	11.16	11.49	12.60	—1.44	11.37	1,090	50.28
Mar. 20-21	3,631	64.9	253.1	246.9	10.38	10.23	11.27	—0.89	8.24	980	50.28
Mar. 21-22	3,467	72.9	209.3	293.7	11.66	12.61	13.78	—2.12	8.96	1,230	50.27
Mar. 22-23	3,281	65.0	226.1	222.2	10.40	12.75	13.79	—3.39	14.52?	946	49.22
Mar. 23-24	3,305	66.1	203.4	278.5	10.58	10.09	11.15	—0.57	8.88	815	49.98
Mar. 24-25	3,466	65.8	225.0	268.9	10.52	9.47	10.52	0.00	6.37	720	50.18
Mar. 25-26	3,591	66.8	227.0	294.1	10.68	9.47	10.54	—0.14	8.00	920	50.24
Mar. 26-27	3,836	66.0	256.2	288.0	10.56	10.03	11.09	—0.53	9.24	880	50.17
Mar. 27-28	3,639	65.6	247.0	261.3	10.50	9.58	10.63	—0.13	3.08	710	49.94
Mar. 28-29	4,194	71.3	269.2	341.0	11.40	10.65	11.79	—0.39	8.13	820	50.00
Mar. 29-30	3,631	81.6	219.1	314.2	13.05	9.72	11.03	+2.02	14.50	930	50.00
Mar. 30-31	3,602	70.2	118.3	302.1	11.23	10.93	12.05	—0.82	24.51	1,040	50.30
Mar. 31- 1	2,922	74.1	162.7	269.6	11.86	11.57	12.76	—0.90	15.90	780	50.30
Apr. 1- 2	3,374	96.1	214.0	363.3	15.38	13.03	14.57	+0.81	11.42	1,100	50.35
Apr. 2- 3	3,366	96.9	200.0	392.5	15.50	12.50	14.05	+1.45	8.20	1,250	50.63

† Urine N plus 10 per cent. of food N.

TABLE 3.—(*Continued*)

Date, 1915	Food					Urine					
	Total Calories	Protein, Gm.	Fat, Gm.	Carbohyd., Gm.	Food N	Urine N	Excreta N, Gm.	N Balance, Gm.	Urine Glucose, Gm.	Urine Vol., c.c.	Body Weight, Kg.
Apr. 5- 6	3,549	89.9	192.4	350.2	14.38	10.78	12.17	+2.21	11.30	970	.....
Apr. 6- 7	3,871	94.2	195.0	407.5	15.07	10.37	11.88	+3.19	8.61	800	50.90
Apr. 7- 8	3,758	98.9	197.5	369.9	15.82	11.71	13.29	+2.53	7.53	910	50.75
Apr. 8- 9	3,908	99.4	193.6	414.7	15.90	11.49	13.08	+2.82	17.22	960	51.15
Apr. 9-10	3,582	99.2	211.0	283.6	15.87	12.05	13.64	+2.23	9.77	1,260	51.33
Apr. 10-11	3,874	98.6	215.4	357.7	14.79	?	.....	......	?	?	51.16
Apr. 14-15	4,109	105.2	195.5	458.6	16.83	11.21	12.89	+3.94	15.65	1,120	51.48
Apr. 15-16	3,303	83.5	195.6	278.6	13.36	11.04	12.38	+0.98	17.0	1,160	.....
Apr. 16-17	3,863	88.4	221.4	351.7	14.14	11.66	13.07	+1.07	14.9	1,390	51.49
Apr. 17-18	3,392	99.6	163.2	157.6	15.94	11.77	13.36	+2.58	.....	1,185	.....
Apr. 18-19	3,623	98.5	179.5	378.1	15.76	11.43	13.01	+2.75	.....	960	51.50
Apr. 19-20	3,494	88.5	166.2	386.5	14.16	12.33	13.75	+0.41	16.4	1,040	51.40
Apr. 20-21	3,769	98.0	181.8	408.8	15.68	12.55	14.12	+1.56	.....	1,050	51.38

* Food approximate on these two days.

Treatment and Course.—For the first twelve days in the hospital he was kept in bed without medication and improved slowly. March 14, after the first observation in the calorimeter, the Forcheimer ergotin and quinin hydrobromate treatment was begun. He continued to improve slowly in general condition, and gained 6 pounds in weight. The blood pressure was 130-65 and 146-66 mm. Hg. The Wassermann reaction was weakly positive; the urine contained a trace of albumin and a few casts. Temperature 99-100, pulse 108-124 up to March 15, then 82-100.

April 8, he was transferred to the surgical wards, and one superior thyroid artery was ligated under local anesthesia. May 2, one inferior thyroid artery was exposed, but the pulse became so rapid and feeble that the wound was hastily sutured without an attempt being made to ligate the vessel. The patient continued to improve slowly. May 14, the left limit of cardiac dulness was 11 cm. to the left of the midline; the murmur was unchanged. The general condition was better than a month before. For clinical data see Table 4.

Notice of his death in February, 1916, has just been received.

Case 4.—*History.*—Dr. G. S. L., aged 52, physician, had typhoid fever twenty-five years ago. He smoked from six to nine cigars a day. His eyes have always been prominent. Three or four years ago when his weight was about 215 pounds, he noticed a slight tremor of the hands and slight dyspnea and palpitation on exertion. About one year ago the neck increased in size. The four thyroid arteries were ligated in January, 1914, (three months ago), but he was nearly exsanguinated by a secondary hemorrhage from the superior thyroid artery. He was given quinin hydrobromate for a month, but developed cinchonism. Thyroidectin in September made him worse. For the last week he has had no treatment.

Physical Examination.—April 9, the patient is 180 cm. in height, tall and large framed. The expression is staring, the skin flushed, warm, moist, smooth, and slightly darkened. Dermatographia is present. There is no hair on the chest. There is moderate protrusio bulbi, slight von Graefe's sign, convergence

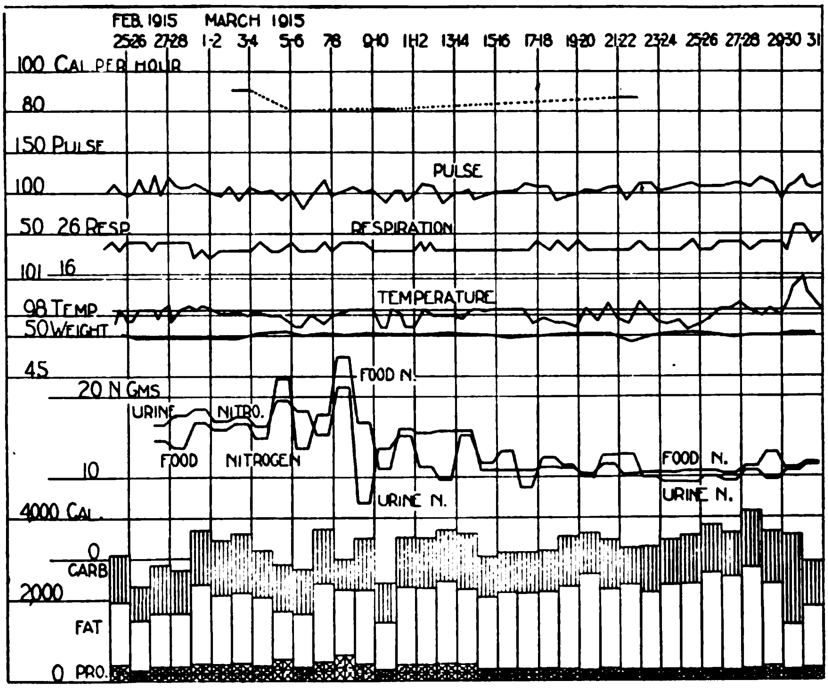

Fig. 3.—Chart in Case 2. Edwin T.

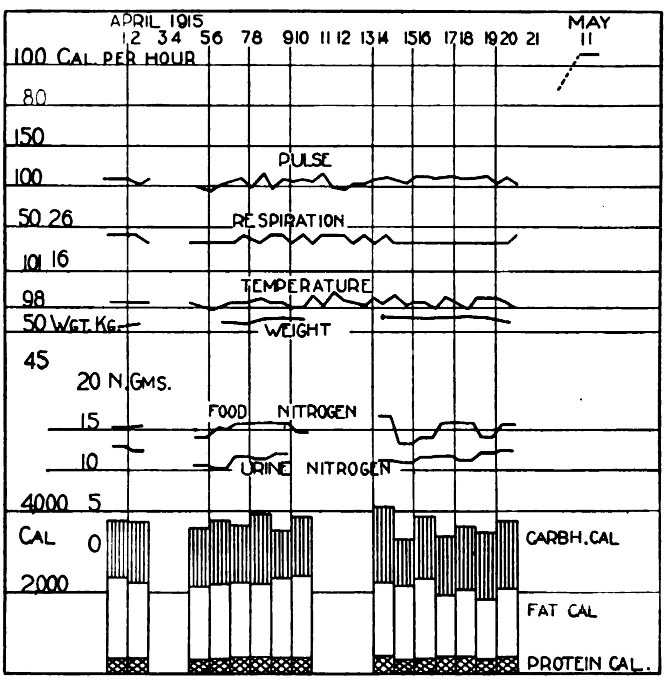

Fig. 4.—Chart in Case 2. Edwin T. (continued)

weak, thyroid lobes and isthmus enlarged. Heart apex impulse is 16 cm. from midline, action regular and heaving. There is a soft systolic murmur maximum in the pulmonic region. Pulse is 100, of large size. Blood pressure is 148 mm. There is a marked tremor of the hands and tongue and also of the legs when standing.

Treatment and Course.—After the calorimeter observation, April 9, the patient was given Dr. Rogers' thyroid "residue," 1 c.c., twice a day until April 16, when he returned for another test, his condition being unchanged except that the heart action was perhaps a little quieter.

In October, 1914, a thyroidectomy was performed. The day after the operation the temperature rose to 101, the pulse to 150, and the respirations to 70 per minute. He died a week later.

TABLE 4.—Clinical Data in Case 3

Date, 1915	Food					Urine					
	Total Calories	Protein, Gm.	Fat, Gm.	Carbohyd., Gm.	Food N	Urine N	Excreta N, Gm. †	N Balance, Gm.	Urine Glucose, Gm.	Urine Vol., c.c.	Body Weight, Kg.
Mar. 9-10	3,322	100.7	183.0	294.5	16.11	11.94	13.55	+2.56	0	1,470	41.39
Mar. 10-11	3,315	94.1	178.7	309.1	15.06	13.51	15.02	+0.04	0	1,380	41.34
Mar. 11-12	3,189	93.7	182.5	270.8	15.00	14.18	15.68	—0.68	0	1,695	41.36
Mar. 12-13	2,558	86.2	145.9	206.9	12.79	15.09	16.47	—3.68	0	1,390	41.16

† Urine N plus 10 per cent. of food N.

Case 5.—*History.*—Peter N., aged 23, with atypical exophthalmic goiter (?), mechanic, admitted April 9, 1915, discharged April 25. His father is 6 feet 4 inches tall (193 cm.). The patient has had sore throat several times. He grew very fast between the ages of 15 and 18. At the age of 18 he became weak and nervous, losing his temper easily. He suffered from severe headaches two or three times a week and his hands grew so tremulous that he has been unable to work for the last year. About a year ago he was in the Massachusetts General Hospital, where his respiratory metabolism was studied by Dr. Means and found to be within normal limits. The superior thyroid arteries were tied, and since then the headaches have been less frequent and the hands drier. He is not much stronger, and he sleeps only two or three hours a night.

Physical Examination.—April 25, 1915, the patient's height is 6 feet 2 inches (187.7 cm.). He is tall and thin with no suggestion of acromegaly. The hands are tapering. The expression is anxious; there are no eye symptoms. The thyroids are soft and slightly enlarged. The hands and feet are sweating, dermatographia marked. Cardiac dulness extends 12 cm. to the left of the midline. Electrocardiograms show a slight respiratory arrhythmia. There is a marked tremor of the right hand and slight tremor of the left. Roentgenoscopy reveals a normal sella turcica. There is a trace of glucose in the urine. During his short stay in the hospital there was no change in his condition. For clinical data see Table 5.

Case 6.—*History.*—Anna K., aged 26, single, born in Ireland, nurse, admitted April 27, 1914, whose mother, one brother and one sister are nervous, had acute rheumatic fever at 16 and has had one attack of severe tonsillitis. For the last ten years she has been high-strung and easily frightened. For several years she has had dyspnea and palpitation on exertion. About December, 1913, all of these symptoms grew worse, and she began to have severe headaches, scanty menses, marked sweating and polyphagia and polydipsia. In February, 1914, she was badly frightened in a runaway, and the symptoms increased in severity. She has lost 15 pounds in weight.

For the last two months she has been given thyroid "residue" by Dr. Rogers. April 4, both superior arteries were ligated by Dr. Rogers in Bellevue Hospital.

Physical Examination.—The patient is very thin, frame small, expression tired and neurotic, speech jerky and agitated, voice weak. Skin moist. Exophthalmos slight, eyelids puffy, no von Graefe's sign, tongue and hands tremulous. Thyroid moderately enlarged, especially on the right. Cardiac impulse diffuse, maximum in the fifth space 8.5 cm. to the left of the midline. Action rapid and regular.

Treatment and Course.—After the first calorimeter observation, the two inferior thyroid arteries were ligated, April 29. May 13, the patient returned to the calorimeter room for the day feeling less nervous and more ambitious than before. June 22, she reported to Dr. Rogers weighing 112 pounds, pulse 90, general condition much improved.

TABLE 5.—Clinical Data in Case 5

Date, 1915	Food					Urine					
	Total Calories	Protein, Gm.	Fat, Gm.	Carbohyd., Gm.	Food N	Urine N	Excreta N, Gm. †	N Balance, Gm.	Urine Glucose, Gm.	Urine Vol., c.c.	Body Weight, Kg.
Apr. 10-11	3,362	85.3	205.4	268.8	13.64	.....	.....	......	.....	.....	63.95
Apr. 14-15	2,330	66.2	137.4	190.5	10.69	12.17	13.28	—2.64	Slight trace	747	63.44
Apr. 15-16	2,898	69.5	170.2	250.1	11.12	12.16	13.27	—2.15	Trace	840	64.00
Apr. 17-18	2,942	87.3	160.6	265.8	13.97	13.84	14.74	—0.87	.....	1,100	.....
Apr. 18-19	2,757	78.2	143.1	274.6	11.71	11.94	13.11	—1.40	.....	1,240	65.18
Apr. 19-20	2,806	72.7	130.5	316.1	11.63	11.94	12.65	—1.02	Trace	1,080	64.64
Apr. 20-21	3,023	74.7	171.6	273.4	11.95	11.49	12.69	—0.74	.....	1,460	65.28
Apr. 21-22	2,714	83.3	149.5	239.6	13.32	11.82	13.13	+0.19	Trace	1,420	64.65
Apr. 22-23	2,465	84.9	137.8	203.7	13.58	12.95	14.31	—0.78	Trace	1,300	64.32
Apr. 23-24	3,006	85.6	189.3	218.1	13.70	12.81	14.18	—1.37	Heavy trace	1,000	64.20
Apr. 24-25	2,847	87.3	174.6	210.9	13.97	12.61	14.01	—0.04	5.21	1,300	64.45

† Urine N plus 10 per cent. of food N.

Case 7.—*History.*—Anna R., aged 29, unmarried, cook and saleswoman, born in Ireland, admitted May 8, 1913, discharged June 5, five years ago had typhoid fever and shortly afterward noticed swelling of her throat. A year or so later her tonsils were removed by a doctor who told her she had a goiter. Since the attack of typhoid she has had at times tremor, palpitation, restlessness and loss of weight. She thinks she has improved during the last two years. A year or so ago her friends noticed that her eyes were staring. She has been able to work up to the time of admission.

Physical Examination.—The patient is tall and thin, exophthalmos present, von Graefe's and Stellwag's signs present. There is slight tremor of hands and tongue. The heart is slightly enlarged, first sound of poor quality. The thyroid is moderately enlarged.

Treatment and Course.—May 8 to 11 temperature is normal, pulse from 84 to 88, respiration from 20 to 22. The first calorimeter observation was on May 10. On the 12th under local anesthesia Dr. Rogers ligated the left superior and right inferior thyroid arteries and removed the tip of the left upper pole. May 16, the two other vessels were ligated and the tip of the right pole removed. After the first operation the temperature was 99 to 100, pulse 100-112, respiration 24 to 26. After the second operation she was given half a grain of the

Loomis Laboratory special thyroid extract every four hours until May 18. She menstruated from May 16 to May 19. For three days after the operation the temperature was 99 to 102, pulse 96-130, respiration 24 to 32. By May 20, at the time of the second calorimeter observation, the temperature was almost normal. By May 25 she was up and about the ward.

After leaving the hospital she spent two months in the country and gained weight up to 117 pounds. Since then she has been at work and has lost 2 pounds, but has not felt nervous except when she works hard. May 14, 1914, she returned for a calorimeter observation. The scars of the operation were well healed, the left lobe and isthmus of the gland were moderately enlarged and the right lobe considerably enlarged. She was still thin and nervous, and the voice weak and husky, but she looked a little better than a year ago.

A week or so after the last calorimeter observation she was married, and did well until her husband lost his job on account of the war. She started work in the store again, and her weight dropped to 104 pounds and all the symptoms returned. In March, 1915, she reported at the ward very thin, very nervous, hands very tremulous, skin moist, pulse very rapid and small.

Case 8.—*History.*—Sarah M., aged 29, chambermaid, unmarried, born in Ireland, admitted April 29, 1914, discharged May 4, nine years ago came to America, and eight years ago began to suffer from loss of weight, nervousness, weakness, tremor and enlargement of the neck. Three months later she was operated on, and apparently part of the thyroid gland removed. She recovered quickly, and for the next six years enjoyed good health. One year ago she began to have a return of the weakness, nervousness and loss of weight. She became excitable, sweated easily, and slept poorly. At times she had palpitation. She thinks the neck has swollen again.

Physical Examination.—April 29, the patient is tall, fairly well nourished, and does not look sick. The eyes are a little brighter than normal, but there is no exophthalmos, no von Graefe's sign and only slight weakness of convergence. The left lobe of the thymus is absent, the right lobe moderately enlarged. There is slight tremor of the tongue and hands on excitement. The heart is not enlarged and is not overacting; pulse from 86 to 97. The skin is a little moist and not flushed.

Treatment and Course.—The afternoon of the calorimeter observation a partial thyroidectomy was performed by Dr. Rogers. She made a rapid recovery, and when she reported in February, 1915, she had no subjective or objective symptoms.

Case 9.—*History.*—Marion B., aged 22, unmarried, admitted Feb. 4, 1915, discharged February 5, was sent down from the Presbyterian Hospital, where her case was studied in detail by Dr. Geyelin. In 1912 the heart began to beat fast, she sweated easily and began to notice swelling of the neck. Four operations were performed at the Presbyterian Hospital. In July, 1913, two arteries were ligated. Two months later the right lobe of the gland was removed. In February, 1914, an appendectomy was necessary. In July, 1914, part of the left lobe of the thyroid was removed, and she felt better until September, 1914, when her nervousness returned. At the time of her admission she had been menstruating four days.

Physical Examination.—The patient is short and rather stout; excitable. She has a nervous, staring, angry expression. The exophthalmos is marked, the pupils are dilated, the skin moist, the pulse small and soft.

Case 10.—*History.*—Margaret L., aged 51, married, with atypical exophthalmic goiter, auricular fibrillation and mitral insufficiency, admitted March 25, 1914, died May 19, 1914. She had three children in good health. A year ago she began to feel nervous, and lost appetite and weight. She noticed a rapidly growing swelling on the right side of the neck. This was removed by operation in July, 1913. Since then she has been worse and has violent palpitation of the

heart all the time. A month ago she began to have huskiness of the voice, swollen arms and legs and much dyspnea.

Physical Examination.—The patient is well developed and well nourished, dull mentally, slow of speech, the voice husky but not brassy. Skin thick, hard, dry, feels myxedematous. Slight exophthalmos, no von Graefe or Stellwagon sign.

Fig. 5 (Case 12).—Benny L. Cretin holding ruler marked in inches.

Right lobe of thyroid absent, left lobe slightly enlarged. Heart much enlarged with an irregularity shown by tracings to be due to fibrillation. There is a systolic murmur at the apex. There is some fluid in the right pleural cavity. She is dyspneic and looks seriously ill.

Treatment and Course.—At first she was given thyroid "residue," but for three weeks before the calorimeter observation received no medication except codein and ammonium carbonate to control the cough. May 5, a small thymus gland was removed. Histologic examination showed "fatty infiltration of the thymus, thymic tissue appears normal." After the operation she developed fever, rapid pulse, grew weaker and died. There was no necropsy.

Case 11.—*History.*—Miss B. H., aged 31, trained nurse, admitted April 4, discharged April 20, 1914. In childhood had pertussis, scarlet fever, measles, varioloid, mumps, bronchitis, typhoid fever at 15 years, appendicitis and peritonitis at 20, many attacks of tonsillitis and finally tonsillectomy at 22, and diphtheria at 29. For the last two or three years she has worked very hard as a nurse on difficult cases.

Fig. 6 (Case 12).—Benny L. Cretin, 36 years old (continued).

In 1910 she noticed that the thyroid was enlarged. In August, 1913, while nursing a typhoid patient she began to have severe diarrhea with eighteen movements a day. She vomited continually, the pulse was very rapid, and she was excitable and weak. After prolonged rest these symptoms would clear up enough to allow her to work once more. In January, 1914, the right side of the thyroid became enlarged and painful, nervousness increased and she lost 20 pounds. In February, 1914, the right lobe of the gland was removed. Two days later the voice, which had been clear, dropped to a whisper, and did not return to normal for a year or so. After the thyroidectomy the pulse rate dropped from an average of 140 to 72, and she has had but little palpitation and no sensation of undue

warmth. The nervousness has begun just as bad, and she has diarrhea whenever she takes fats. At the time of admission to Bellevue she was much depressed over the loss of her voice, which she feared was to be permanent.

Physical Examination.—April 4, 1914, the patient is of moderate height (159.2 cm.), thin, looks tired and nervous, at times excitable, but always anxious to cooperate in treatment or observations. There is a very slight exophthalmos, slight widening of the palpebral fissure, eyes bright, no von Graefe's sign. There is no enlargement of the isthmus or remaining lobe. The heart is normal and not rapid. There is no dermatographia but at times there is tremor.

Fig. 7 (Case 12).—Benny L. Roentgenogram of hand.

Treatment and Course.—While in the hospital she was very nervous, slept poorly, and at times vomited. The temperature was normal, pulse 72 to 92, respiration 22 to 26. Until the completion of the second calorimeter observation, April 13, she received no medicine, then thyroid "residue," 1 c.c. hypodermically twice a day until the third test. While in the hospital on a low diet containing about 4 gm. of nitrogen the urinary nitrogen was from 3 to 4 gm. a day.

After leaving the hospital she went to the country, and her appetite improved and she gained strength and did well except for a sudden severe stomatitis which loosened her teeth. In March, 1915, she reported looking thin but almost well. She is able to do light work nursing if she rests between cases. Her physician now attributes many of her symptoms during the past year to hysteria.

Case 12.—*History.*—Benny L., aged 36 (?), with cretinism, Hebrew, admitted April 8, 1914, discharged May 2, was taken to the Children's Hospital on Ran-

dall's Island sixteen years ago, and during that time has had no visitors, so that his previous history is unknown. He has not changed since his admission, and he is very happy playing with the boys and going to school, where he learns practically nothing. He can write his name, dress and feed himself and he corresponds to a child of about 7 years in the Binet test. In 1906 an attempt was made to transplant sheep's thyroid into the pelvis of the left kidney and later into the abdomen. There were no favorable results. He has had numerous courses of treatment with Parke, Davis & Co. thyroid extract, but on doses as small as from one-half to 1 grain three times a day develops tachycardia, weakness and often faints.

TABLE 6.—CLINICAL DATA IN CASE 12 (BENNY L.)

Date	Temperature		Total Calories	Carb., Gm.	Fat, Gm.	Food N.	Urine, N.	Body Weight	Urine, Volume, c.c.
	Min.	Max.							
4/ 8/14	....	99.2	.....	.....	.....	....	....	.....	.....
9/ 9/14	98.4	98.6	2,381	229.0	120.0	12.5	7.90	.....	1,200
4/10/14	98.4	98.4	1,118	112.0	53.0	6.6	5.95	23.19	965
4/11/14	98.2	98.2	1,227	125.0	56.0	7.7	6.19	.....	920
4/12/14	98.2	98.2	1,396	140.0	65.0	8.4	6.66	.....	1,000
4/13/14	98.2	98.2	1,496	152.0	70.0	8.7	6.89	.....	1,070
4/14/14	98.6	99.4	1,129	162.0	37.0	4.8	4.67	23.34	795
4/15/14	98.2	98.4	1,360	187.0	63.0	8.2	3.58	.....	710
4/16/14	98.4	99.0	1,229	130.0	55.0	7.3	6.36	.....	950
4/17/14	97.6	98.2	1,084	100.0	51.0	5.9	5.83	24.21	935
4/18/14	97.8	98.0	1,128	109.0	55.0	6.8	5.16	.....	800
4/19/14	98.0	98.6	974	94.0	47.0	5.8	7.01	.....	1,195
4/20/14	98.0	98.2	1,196	117.0	57.0	6.9	6.11	.....	1,195
4/21/14	98.0	98.8	648	66.0	23.0	6.1	5.39	24.06	970
4/22/14	98.0	98.6	1,187	119.0	54.0	7.8	6.19	.....	900
4/23/14	98.0	98.2	704	57.0	33.0	4.4	4.82	24.30	770
4/24/14	97.6	98.0	1,050	108.0	50.0	6.5	5.05	.....	815
4/25/14	97.8	98.6	1,187	135.0	50.0	6.4	5.60	.....	1,040
4/26/14	98.6	98.6	963	108.0	44.0	5.0	4.61	.....	820
4/27/14	98.0	98.6	839	128.0	25.0	3.2	4.13	23.61	672
4/28/14	98.0	98.6	728	68.0	36.0	4.5	4.04	.....	700
4/29/14	98.6	100.0	618	59.0	31.0	3.5	5.32	.....	1,350
4/30/14	99.6	100.2	1,061	99.0	53.0	6.3	6.11	.....	1,400
5/ 1/14	100.2	101.0	856	87.0	17.0	...	....	23.06	.....

Physical Examination.—The patient (Figs. 5-7) is short, 110.3 cm. tall (3 feet 7½ inches), stout, with prominent abdomen, short, trick extremities and short pudgy hands, the face is broad, wrinkled, with thick lips, broad nose, baggy eyelids, teeth widely spaced, in poor condition with much gingivitis and pyorrhea. The thyroid is not palpable, heart normal, abdomen shows slight umbilical hernia. Scars over right kidney, skin very dry, harsh, inelastic with fine branny desquamation. There are pads of fat on each side of the neck, and others just anterior to axillae. External genitals resemble those of a boy of 7; there are no male secondary sexual characteristics. Blood pressure is 125 mm., Wasser-

mann test strongly positive; the urine contains much sterile pus, evidently due to large calculi shown by roentgenoscopy to be in the pelves of the kidneys. The temperature was slightly subnormal most of the time, pulse 64-80, respiration 18.

The patient was always in good humor. He had a good sense of fun and was a natural clown, his voice was hoarse and childish but he differed from the normal child in being able to sit quiet for hours at a time. He grew tired rather easily, his appetite was very small, his bowels constipated. April 27, in the afternoon, the administration of thyroid extract was begun, 1 grain three times a day; the temperature rose to the level of 100 F, pulse 100, respiration 18, blood pressure 115. He felt limp, and looked sick so that the drug had to be discontinued. For clinical data see Table 6.

Discussion of Results

THE BASAL METABOLISM IN EXOPHTHALMIC GOITER

The determination of the basal metabolism in exophthalmic goiter is a matter of technical difficulty. The patients are excitable, restless and easily tired. For this reason great care must be used when nose or mouthpieces or face masks are employed, since these may prove uncomfortable toward the end of an experiment or series of experiments. The respiration calorimeter, although perfectly comfortable for a normal person for five hours, often tires a goiter patient after three hours. Fortunately the apparatus is so delicate and accurate that the measurement of the heat production by the method of indirect calorimetry is satisfactory after a preliminary period of three-fourths hour. Experiments one hour long could be employed, but two hour observations are more satisfactory since the method of direct calorimetry is not as accurate as could be wished in the first experimental hour. This will be discussed later.

There is a distinct tendency for the patients to become more restless as the observation progresses, and it will be noted that the metabolism in the fasting experiments is usually higher in the second hour than in the first. There is also a tendency on the part of patients as well as normal controls to show a slightly higher metabolism the first time they are the subject of a real experiment, although they are all trained by a short "dummy experiment" a day or so previously. Goiter patients on some days are distinctly more disquieted than usual, and one gets the impression that on such days the increase in metabolism is due partly to the restlessness and partly to an exacerbation of the disease which causes both restlessness and increased heat production.

It has long been realized that tremor and involuntary activity on the part of goiter patients might be responsible for a considerable portion of the increase in metabolism. Magnus-Levy discussed these factors, and found that the increase in metabolism is almost as marked when the patient is sleeping or under the effect of opium. He found also that the tremor of paralysis agitans increased the oxygen consumption only from 20 to 30 per cent. A careful scrutiny of the

results reported in the present work shows that restlessness, tremor and mental irritability contribute only a small percentage of the increase in most of the cases. The activity of the patients was checked by the delicate work-adder and by careful observation. All of the patients

TABLE 7.—The Influence of Sleep, Restlessness, Etc., on Metabolism in Hourly Periods

Subject and Date	Calories per Hour Ind.	Per Cent. above Lowest Figure	Work-Adder Cm.	Behavior of Patient
Case 1 (Max W.)				
Feb. 16	114.6	..	31	A little restless; involuntary tremor at end of period
	124.1	9	14	A little restless
Feb. 20	104.9	..	16	Calm and quiet
	114.2	9	22	Calm; slightly excited by visitor for ten minutes
Feb. 21	120.8	8	26	After dextrose; quiet
	117.2	..	55	After dextrose; very restless
Mar. 4	101.1	..	15	Asleep the whole hour
	106.2	5	58	Awake, pulse rapid last half hour
April 6	92.2	..	25	Quiet; asleep 50 minutes
	99.4	8	55	Very restless
	101.4	10	51+	Very restless; uncomfortable
April 23, 1915	102.8	..	21	Fairly quiet; asleep 30 minutes
	111.0	8	83	Fairly quiet; asleep 5 minutes
Case 2 (Edwin T.)				
Mar. 3	93.6	5	23	Quiet, reading 45 minutes
	89.2	..	30	Asleep 50 minutes in 90-minute period
Mar. 6	80.2	0	6	Reading whole hour; very quiet
	80.2	..	19	Asleep 55 minutes; fairly quiet
Mar. 10	75.4	..	16	Sleeping; slightly restless
	87.3	16	18	Reading 55 minutes
Mar. 22	79.8	..	?	Sleeping; very quiet
	88.0	11	10	Reading 55 minutes; quiet
	94.8	20	30	Asleep
May 11	96.2	..	15	Restless; stretched arms
	115.1	20	34	Restless; vomited shortly after exp.
Case 3 (James McE.)				
Mar. 12	95.8	..	14	Reading quietly 50 minutes
	98.6	3	23	Reading quietly 36 minutes
	101.7	6	30	Not reading; fairly quiet
Mar. 31	88.6	..	10	Reading 60 minutes; quiet
	95.6	8	26	Reading 32 minutes; restless
Case 4 (Dr. G. S. L.)				
April 16	104.8	..	29	Fairly quiet
	109.3	4	58	Slightly restless
Case 6 (Anna K.)				
April 23	102.6	1	36	Restless
	101.5	..	38	Quieter

were as quiet as the normal controls for at least some of the periods of observation. Most of them slept quietly during a considerable portion of some periods. When we compare the sleeping and quiet periods with those in which the patient was awake or excited or restless, we find no constant and striking increase large enough to change our inter-

TABLE 8.—SUMMARY OF RESULTS OF RESPIRATION EXPERIMENTS

Subject and Date	Character of Experiment	Average Pulse Rate	Average R. Q.	Per Cent. Divergence of Direct from Indirect Calorimetry	Indirect Calorimetry Average Calories per Hour					Per Cent. Rise above Patient's Own Basal Metabolism	Day of Basal Determination Used for Comparison	Remarks
					Per Kg.	Per Sq. M. Meeh	Per Cent. Rise above Average Normal Basal 34.7 Meeh	Per Sq. M. Linear	Per Cent. Rise above Average Normal Basal 39.7 Linear			
Case 1 (Max W.) 2/16/14	Basal	137	0.76	— 4	1.98	62.0	+79	69.4	+75	....	....	Slightly restless
2/18/14	¾ to 3¾ hrs. after 100 dextrose	124	0.90	— 1	1.79	57.7	....	64.7	....	+ 2	Av. Feb. 20, 27, Mar. 4	Slightly restless
2/20/14	Basal	111	0.77	— 4	1.78	57.0	+64	63.7	+60	....	....	Quiet
2/21/14	¾ to 2¾ hrs. after 100 dextrose	105	0.94	— 5	1.91	61.5	....	68.8	....	+ 9	Av. Feb. 20, 27, Mar. 4	Restless 1 hour
2/25/14	1½ to 3½ hrs. after 8.9 N as casein	138	0.88	— 3	2.02	64.7	....	71.9	....	+14	Av. Feb. 20, 27, Mar. 4	Quiet
2/27/14	Basal	136	0.77	— 2	1.83	58.4	+68	65.4	+65	....	....	Restless 1 hour
3/ 2/14	1½ to 3½ hrs. after 9.0 N as meat	101	0.82	+ 3	1.87	59.6	....	66.5	....	+ 5	Av. Feb. 20, 27, Mar. 4	Quiet
3/ 4/14	Basal	108	0.77	— 2	1.73	54.9	+58	61.0	+54	....	....	Asleep 1 hour; restless 1 hour
3/23/14	Basal	87	0.77	+ 4	1.57	49.7	+43	55.3	+39	....	....	Quiet; dozed
4/ 6/14	Basal	95	0.79	+ 1	1.59	51.0	+47	57.1	+44	....	....	Restless
4/24/14	Basal	120	0.78	+ 1	1.69	54.4	+57	60.9	+53	....	....	Restless
4/23/15	Basal 1 yr. later	99	0.77	— 4	1.46	49.6	+43	57.7	+45	....	....	Quiet; dozed
Case 2 (Edwin T.) 3/ 3/15	Basal	99	0.78	— 4	1.84	54.9	+58	61.7	+55	....	....	Slightly restless
3/ 5/15	2 to 6 hrs. after 8.95 N as casein	88	0.86	— 4	1.78	53.4	+54	60.6	+53	+ 7	Av. Mar. 3, 6 and 10	Quiet
3/ 6/15	Basal	87	0.81	+ 4	1.60	47.9	+38	53.8	+37	....	....	Quiet
3/ 8/15	2 to 5 hrs. after 10.19 N as meat	95	0.82	— 6	1.88	56.2	62	63.4	....	+11	Av. Mar. 3, 6 and 10	Quiet
3/10/15	Basal	92	0.80	—12	1.65	49.1	+42	55.3	+39	....	....	Quiet
3/22/15	Basal	107	0.79	— 3	1.71	52.8	+52	59.4	+50	....	....	Quiet
5/11/15	Basal 2 to 3 weeks after ligation	134	0.76	— 4	2.10	63.0	+82	71.2	+79	....	....	Slightly restless

Case 3 (James McE.) 3/12/15	Basal	109	0.78	− 6	2.40	67.2	+94	74.4	+87	....	....	Quiet
3/31/15	Basal after quinin and ergotin	97	0.82	− 4	2.30	64.0	+84	70.7	+78	....	....	Fairly quiet
5/14/15	Basal after ligation	115	0.75	− 8	2.30	68.1	+97	76.1	+92	....	....	Fairly quiet
Case 4 (Dr. G. S. L.) 4/ 9/14	Basal	100	0.77	− 0	1.45	46.9	+42	55.0	+88	....	....	Quiet
4/16/14	Basal after thyroid "residue"	99	0.76	− 4	1.54	51.5	+50	57.6	+45	....	....	Slightly restless
Case 5 (Peter N.) 4/14/15	Basal	71	0.83	+ 8	1.10	35.5	+ 2	38.8	− 2	....	....	Very quiet
Case 6 (Anna K.) 4/28/14	Basal after ligation of 2 arteries	121	0.75	− 5	2.30	66.1	+104	....	....	....	....	Fairly quiet
5/13/14	Basal after ligation of 2 more arteries	100	0.81	− 8	1.90	55.1	+71	....	....	....	....	Very quiet
Case 7 (Anna R.) 5/10/13	Basal	119	0.79	− 8	1.45	43.4	+34					
5/20/13	Basal after ligation	...	0.76	− 7	1.79	49.9	+55	....	....	....	....	Quiet
5/28/13	Basal	...	0.77	− 5	1.64	49.2	+52					
5/14/14	Basal 1 yr. later	97	0.80	− 4	1.48	43.6	+35	....	....	....	....	Very quiet
Case 8 (Sarah M.) 4/29/14	Basal*	92	0.78	− 4	1.41	43.8	+36	....	....	....	....	Fairly quiet
Case 9 (Marion B.) 2/5/15	Basal	127	0.77	− 1	1.40	44.1	36	....	....	....	....	Restless
Case 10 (Mrs. L.) 4/20/14	Basal	85	0.76	− 1	1.30	42.0	30					
Case 11 (Miss B. H.) 4/ 8/14	Basal	60	0.83	+ 4	1.21	35.4	+10	40.0	+ 8	....	....	Quiet
4/13/14	Basal	74	0.81	− 1	1.19	35.1	+ 9	39.9	+ 8	....	....	Very quiet
4/18/14	Basal after thyroid "residue"	94	0.84	− 2	1.15	33.4	+ 8	37.8	+ 2	....	....	Very quiet
Case 12 (Benny L.) 4/10/14	Basal	84	0.92	+ 8	1.21	27.6	−20	33.0	−17	....	....	Very quiet
4/14/14	1 to 4 hrs. after 100 dextrose	88	1.00	− 1	1.34	31.4	....	37.9	....	+15	April 10	Very quiet
4/21/14	1½ to 5½ hrs. after 3.6 N casein	82	0.98	+ 6	1.23	28.9	....	34.9	....	+13	April 23	Quiet
4/23/14	Basal	78	0.87	− 0	1.09	25.6	−26	31.0	−22	....	....	Quiet
4/27/14	1 to 4 hrs. after 70 dextrose	79	0.95	+ 0	1.19	27.7	....	33.3	....	+ 7	April 23	Very quiet
5/ 1/14	After thyroid extract	95	0.79	− 6	1.44	33.2	− 4	39.8	+ 0	+28	April 23	Very quiet

* After very small breakfast.

TABLE 8.—Summary of Results of Respiration Experiments

Subject and Date	Character of Experiment	Average Pulse Rate	Average R. Q.	Per Cent. Divergence of Direct from Indirect Calorimetry	Indirect Calorimetry Average Calories per Hour: Per Kg.	Per Sq. M. Meeh	Per Cent. Rise above Average Normal Basal 34.7 Meeh	Per Sq. M. Linear	Per Cent. Rise above Average Normal Basal 39.7 Linear	Per Cent. Rise above Patient's Own Basal Metabolism	Day of Basal Determination Used for Comparison	Remarks
Case 1 (Max W.)												
2/16/14	Basal	137	0.76	− 4	1.98	62.0	+79	69.4	+75	....	....	Slightly restless
2/18/14	¾ to 3¾ hrs. after 100 dextrose	124	0.90	− 1	1.79	57.7	....	64.7	....	+ 2	Av. Feb. 20, 27, Mar. 4	Slightly restless
2/20/14	Basal	111	0.77	− 4	1.78	57.0	+64	63.7	+60	....	....	Quiet
2/21/14	¾ to 2¾ hrs. after 100 dextrose	105	0.94	− 5	1.91	61.5	....	68.8	....	+ 9	Av. Feb. 20, 27, Mar. 4	Restless 1 hour
2/25/14	1½ to 3½ hrs. after 8.9 N as casein	138	0.83	− 8	2.02	64.7	....	71.9	....	+14	Av. Feb. 20, 27, Mar. 4	Quiet
2/27/14	Basal	136	0.77	− 2	1.83	58.4	+68	65.4	+65	....	....	Restless 1 hour
3/ 2/14	1½ to 3½ hrs. after 9.0 N as meat	101	0.82	+ 3	1.87	59.6	....	66.5	....	+ 5	Av. Feb. 20, 27, Mar. 4	Quiet
3/ 4/14	Basal	108	0.77	− 2	1.73	54.9	+58	61.0	+54	....	....	Asleep 1 hour; restless 1 hour
3/23/14	Basal	87	0.77	+ 4	1.57	49.7	+43	55.3	+39	....	....	Quiet; dozed
4/ 6/14	Basal	95	0.79	+ 1	1.59	51.0	+47	57.1	+44	....	....	Restless
4/24/14	Basal	120	0.78	+ 1	1.69	54.4	+57	60.9	+53	....	....	Restless
4/28/15	Basal 1 yr. later	99	0.77	− 4	1.46	49.6	+43	57.7	+45	....	....	Quiet; dozed
Case 2 (Edwin T.)												
3/ 3/15	Basal	99	0.78	− 4	1.84	54.9	+58	61.7	+55	....	....	Slightly restless
3/ 5/15	2 to 6 hrs. after 8.95 N as casein	88	0.86	− 4	1.78	53.4	+54	60.6	+53	+ 7	Av. Mar. 3, 6 and 10	Quiet
3/ 6/15	Basal	87	0.81	+ 4	1.60	47.9	+38	53.8	+37	....	....	Quiet
3/ 8/15	2 to 5 hrs. after 10.19 N as meat	95	0.82	− 6	1.88	56.2	62	63.4	....	+11	Av. Mar. 3, 6 and 10	Quiet
3/10/15	Basal	92	0.80	−12	1.65	49.1	+42	55.3	+39	....	....	Quiet
3/22/15	Basal	107	0.79	− 3	1.71	52.8	+52	59.4	+50	....	....	Quiet
5/11/15	Basal 2 to 3 weeks after ligation	134	0.76	− 4	2.10	63.0	+82	71.2	+79	....	....	Slightly restless

Case 3 (James McE.) 3/12/15	Basal.................	109	0.78	— 6	2.40	67.2	+94	74.4	+87	....	....	Quiet
3/31/15	Basal after quinin and ergotin	97	0.82	— 4	2.30	64.0	+84	70.7	+78	....	....	Fairly quiet
5/14/15	Basal after ligation...	115	0.75	— 8	2.30	68.1	+97	76.1	+92	....	....	Fairly quiet
Case 4 (Dr. G. S. L.) 4/ 9/14	Basal.................	100	0.77	— 0	1.45	46.9	+42	55.0	+88	....	....	Quiet
4/16/14	Basal after thyroid "residue"	99	0.76	— 4	1.54	51.5	+50	57.6	+45	....	....	Slightly restless
Case 5 (Peter N.) 4/14/15	Basal.................	71	0.83	+ 8	1.10	35.5	+ 2	38.8	— 2	....	....	Very quiet
Case 6 (Anna K.) 4/28/14	Basal after ligation of 2 arteries	121	0.75	— 5	2.30	66.1	+104	....	....	....	....	Fairly quiet
5/13/14	Basal after ligation of 2 more arteries	100	0.81	— 8	1.90	55.1	+71	....	....	....	....	Very quiet
Case 7 (Anna R.) 5/10/13	Basal.................	119	0.79	— 8	1.45	43.4	+34					
5/20/13	Basal after ligation...	...	0.76	— 7	1.79	49.9	+55	....	....	....	....	Quiet
5/28/13	Basal.................	...	0.77	— 5	1.64	49.2	+52					
5/14/14	Basal 1 yr. later.......	97	0.80	— 4	1.48	43.6	+35	....	....	....	....	Very quiet
Case 8 (Sarah M.) 4/29/14	Basal*................	92	0.78	— 4	1.41	43.8	+36	....	....	....	....	Fairly quiet
Case 9 (Marion B.) 2/5/15	Basal.................	127	0.77	— 1	1.40	44.1	36	....	....	....	....	Restless
Case 10 (Mrs. L.) 4/20/14	Basal.................	85	0.76	— 1	1.30	42.0	30					
Case 11 (Miss B. H.) 4/ 8/14	Basal.................	60	0.83	+ 4	1.21	35.4	+10	40.0	+ 8	....	....	Quiet
4/13/14	Basal.................	74	0.81	— 1	1.19	35.1	+ 9	39.9	+ 8	....	....	Very quiet
4/18/14	Basal after thyroid "residue"	94	0.84	— 2	1.15	33.4	+ 3	37.8	+ 2	....	....	Very quiet
Case 12 (Benny L.) 4/10/14	Basal.................	84	0.92	+ 8	1.21	27.6	—20	33.0	—17	....	....	Very quiet
4/14/14	1 to 4 hrs. after 100 dextrose	88	1.00	— 1	1.34	31.4	....	37.9	....	+15	April 10	Very quiet
4/21/14	1½ to 5½ hrs. after 3.6 N casein	82	0.98	+ 6	1.23	28.9	....	34.9	....	+18	April 23	Quiet
4/23/14	Basal.................	78	0.87	— 0	1.09	25.6	—26	31.0	—22	....	....	Quiet
4/27/14	1 to 4 hrs. after 70 dextrose	79	0.95	+ 0	1.19	27.7	....	33.3	....	+ 7	April 23	Very quiet
5/ 1/14	After thyroid extract	95	0.79	— 6	1.44	33.2	— 4	39.8	+ 0	+28	April 23	Very quiet

* After very small breakfast.

pretation of the results. All of the experiments which show significant differences between the various periods either in the heat-production, work-adder reading or activity of the patient as noted in the protocol have been grouped in Table 7. Some of the patients were allowed to read while in the calorimeter, since it was found that they were quieter if their minds were pleasantly occupied. It will be seen that the metabolism was about the same during the reading periods as during the periods of slightly restless slumber characteristic of this disease. Edwin T. (Case 2) was the only subject who showed an increase of more than 10 per cent. on account of movement. On March 10, reading seemed to increase the calories 16 per cent. March 22, the reading metabolism is about half way between that of two widely varying sleeping periods, and May 11 it rose on account of nausea in the last period.

The results of all the respiration experiments are summarized in Table 8, and the average metabolism on the days of the basal determinations compared to the normal averages discussed in the thirteenth paper of this series. It will be noted that in all the thin patients the rise above the normal is less marked when the measurements are made according to the linear formula than if Meeh's formula for the determination of the surface area be employed. If we confine our attention for the time being to the basal metabolism during the first week that the patients were in the hospital, we can compare the cases here reported with those already described in the literature. In all there is a total of forty-five patients whose respiratory metabolism has been studied, fasting and as quiet as the circumstances would permit. It has seemed best to group these in Table 1 arranging them according to the calories per square meters of surface area as calculated from Meeh's formula. The calculation of the calories has been made from the tables of Magnus-Levy,[26] using the oxygen consumption and respiratory quotient, assuming that protein furnished about 15 per cent. of the calories. This gives a more accurate basis of comparison than the mere statement of cubic centimeters of oxygen or carbon dioxid per kilogram and minute. Still better comparisons might be made if we could use the linear formula or its modification; but this is impossible because many of the authors do not give the heights of the patients. We are similarly handicapped in the tabulation of other symptoms, since many of the clinical reports are very brief. Still it is possible to make a fairly complete chart which allows us to see which symptoms accompany the cases with high metabolism. The plus marks are necessarily my own interpretation of the author's statements.

26. Magnus-Levy: Von Noorden's Handbuch der Pathologie des Stoffwechsels, Ed. 2, 1906, i, 207.

At the head of the list comes Hirschlaff's patient Louise B. shortly before her death with the most extreme symptoms of hyperthyroidism. There are eight other subjects whose metabolism is greater than 56.5 calories per square meter per hour, a figure 75 per cent. above the average for women. Of these all are classified as severe or very severe, except one designated "ziemlich schwer." All show a very rapid pulse, thyroid enlargement, exophthalmos, mental irritability, warmth of skin, tremor and emaciation. Eleven more patients are above the figure which represents a 50 per cent. increase in metabolism. Of these, one is classified as very severe, five are classified as severe, and five as moderately severe. With most of these the pulse rate averages over 100 and there are signs of cardiac enlargement. Goiter, mental irritability, tremor and warmth of skin are present in all. Exophthalmos is absent in one, and the emaciation is slight as a rule.

The figure 38.2 represents the upper normal limit for men, and 35.5 that for women. Between these marks and that indicating a 50 per cent. increase there are sixteen patients, six severe, one moderately severe, four mild, and the others atypical, "forme fruste" or simple goiter. In them the tachycardia is not so marked, and exophthalmos and emaciation are inconstant. Goiter, mental irritability, tremor and warmth of skin are present. There are eight subjects within normal limits. Among these are four mild cases of exophthalmic goiter, two of simple goiter, and two cases in which operation had been performed, one of these being atypical from the start. One patient is below the normal limit. Magnus-Levy in one article classifies her case as half way between Kropf and "forme fruste," and in another article as simple goiter and refers to her as hysterical.

Age is a factor which changes our interpretation of some of the results. The boy M. P., aged 11½ years, with a small struma, is really a little below the average level for his age. Frau B. and Frl. U., aged 52 and 55, respectively, are at an age when the normal metabolism is from 5 to 10 per cent. lower than the average figure for younger women.

The patients whose metabolism is within or below the normal limits show but slight tachycardia, slight if any goiter or exophthalmos and no unusual warmth of skin. Two show mental irritability and tremor.

We must not forget that some of the symptoms of hyperthyroidism are due either wholly or in part to the increased metabolism. The sensation of unusual warmth, the hot, flushed skin and the sweating are caused by the fact that each square centimeter of skin must radiate more heat than in a normal person. These phenomena are found with an increased metabolism from almost any cause, although it is quite possible that in exophthalmic goiter they may be more marked for the same degree of increase. In like manner the loss of

weight is due to the fact that the increased heat production is not balanced by an increased caloric intake and absorption. The appetite of the goiter patient would keep the weight stationary or even cause an increase were the metabolism normal. For some reason the appetite and absorptive powers in hyperthyroidism are not quite sufficient to maintain weight, although laboring men with a much higher caloric requirement per day remain in nutritive equilibrium. This may be accounted for in part by the increased nitrogen metabolism, which is usually ascribed to a toxic destruction of protein. Part of the increase in pulse rate is also due directly to the increased metabolism which necessitates a greater blood flow. This, however, would not account for all of the increase, since muscular work, raising the metabolism from 50 to 100 per cent., seems to increase the pulse rate by only 10 to 30 beats per minute. Still we must remember in discussing the tachycardia and cardiac enlargement that the continued stimulation of metabolism in hyperthyroidism is very different from the stimulation due to muscular exercise which lasts for only a fraction of a day. If it were possible to stimulate the metabolism of a normal man twenty-four hours a day over the period of a year or more, we might perhaps reproduce the cardiac symptoms of hyperthyroidism as well as the warmth of skin and loss of weight.

The more we study the table, the more apparent it becomes that the increase in metabolism is proportional to the severity of the disease. The only exceptions in the group are found in doubtful or atypical cases, or those that have undergone operative treatment. Very severe cases show a metabolism 75 per cent. or more above the average, severe cases 50 per cent. or more, moderately severe and mild cases show an increase of less than 50 per cent., while a few mild and several atypical or cases in which operation has been performed are within normal limits. The degree of tachycardia, goiter, exophthalmos and mental irritability are roughly proportional to the increased heat production. Unfortunately we have not enough data to compare the level of metabolism with the degree of mononucleosis, the sugar tolerance, the drop in blood pressure from large vessels to the periphery, the eye sympoms and many others that are considered of prime importance by various authors.

THE RESPIRATORY QUOTIENTS

In the patients with high basal metabolism, the respiratory quotients are necessarily low after a fast of seventeen hours or more. Most of them are close to the figure of 0.77, which indicates that about 17 per cent. of the calories are derived from the combustion of carbohydrates. With normal men the quotient under similar conditions varies rather widely, but averages 0.82, showing that about 32 per

cent. of the calories are derived from carbohydrates. Therefore goiter patients who are kept in bed in the hospital evidently have less available glycogen after a fast of seventeen hours than normal men who have been up and about during the evening and morning before the experiment. This may be due either to the fact that the thyroid patients have insufficient appetites and start the evening with a smaller store of glycogen, or else that they use up the starch of the food and the stored glycogen more rapidly than the controls. The respiratory quotients here reported give no indication of any qualitative change in the metabolism. The lowest average basal quotient is 0.75, and this is exactly what might be expected in patients with exceedingly high metabolism. In Case 1 (Max W.) the quotients rose to 0.94 on one day and 0.98 on another after the ingestion of 100 gm. of dextrose. The latter figure shows that 89 per cent. of the calories was being derived from carbohydrate from two to three hours after the sugar was taken. The urine passed immediately afterward contained 3.9 gm. glucose, but it is evident that this glycosuria was not due to any impairment of the power to metabolize carbohydrates. The explanation must be sought in an abnormality of mobilization. Cramer and Krause[27] show that after the ingestion of thyroid substance the liver no longer retains glycogen as before.

DIRECT AND INDIRECT CALORIMETRY

One contribution to the science of metabolism which can be made only by a respiration calorimeter is a comparison of the direct and indirect calorimetry. The former method depends on the direct measurement of the heat of radiation, conduction and vaporization. The latter depends on the measurement of carbon dioxid and oxygen and the calculation of the foodstuffs metabolized each hour. It has been shown in the fourth paper of this series that the two methods agree within 0.17 per cent. when normal controls are studied in periods lasting three hours or more. In the seventh paper it was shown that the method of direct calorimetry gave a total which was 2.2 per cent. less than the indirect total in typhoid fever, and that the average divergence of the two methods in the individual experiments was 5 per cent. In the cases of hyperthyroidism here reported, the total number of calories measured is 8,052 according to the indirect method, and 7,823 according to the direct method, which is 2.9 per cent. lower. The individual experiments show that the average divergence is $\pm$ 4.1 per cent. With the cretin Benny L., the direct calorimetry was 1.5 per cent. higher than the indirect. When one considers the technical difficulty of making short respiration chamber experiments on sick patients, the close agreement of two absolutely independent methods is very

27. Cramer and Krause: Proc. Roy. Soc. London, 1913, B., lxxxvi, 550.

striking. The fact that the direct calorimetry is slightly lower can be ascribed to technical errors in the direct method, which have been discussed in previous papers. It may be due to an unmeasured loss of heat to the bed and bed clothing or to an error in the measurement of the average temperature change of the body. The effect of these errors is minimized in long experiments such as are used in normal controls, but it is necessary to use short experiments with patients. The slight disagreement does not point to any disturbance of the intermediary metabolism. The law of the conservation of energy holds good in exophthalmic goiter.

WATER ELIMINATION THROUGH SKIN AND LUNGS

In the thirteenth paper of this series it was shown that under the atmospheric conditions prevailing in the calorimeter experiments, normal men eliminated on an average 28.4 gm. of water an hour through skin and lungs. Of the total calories produced, the average percentage dissipated through vaporization of water was 23.9. Few of the experiments showed a deviation of more than 10 per cent. from this mean.

In hyperthyroidism the heat production and water vaporization are both increased, and in Table 9 we see that they are increased in almost equal proportion. The average water elimination of the severe and moderately severe cases is 39.9 gm. per hour. On an average, 25.7 per cent. of the heat is dissipated through vaporization, or almost the same as in the normal controls. The percentage rise in water elimination through skin and lungs would seem to be a valuable guide as to the extent of the rise in total metabolism.

SPECIFIC DYNAMIC ACTION OF PROTEIN AND DEXTROSE

Owing to the variations in the basal metabolism of goiter patients, the results of this part of the investigation are not as clear cut as might be desired. In Table 10 the figures obtained on Max W. (Case 1), Edwin T. (Case 2) and the little cretin, Benny L. (Case 12) are given. It is difficult to select the proper basis of comparison for these three groups. Should we use the same actual amount of food, the same amount per kilogram, per square meter of body surface or per calories metabolized per hour? Should we compare the results in terms of percentage increase in metabolism or in the terms of extra calories? In the two exophthalmic goiter cases the protein meals produced almost exactly the same percentage rise as in the normal controls. With Max W. (Case 1) the metabolism was higher after the meal containing the protein in the form of casein and egg albumin than after the same amount of protein as found in beef. Edwin T. (Case 2) showed just the opposite, but the meat contained more

TABLE 9.—WATER ELIMINATION OF GOITER PATIENTS: BASAL EXPERIMENTS

Subject and Date	Average Water, Gm. per Hour	Average Calories per Hour, Dir. Calor.	Per Cent. Calories Lost through Vaporization
Case 1 (Max W.)			
Feb. 16, 1914	45.33	114.40	29.16
Feb. 20, 1914	40.95	105.52	22.67
Feb. 27, 1914	41.48	109.34	22.16
Mar. 4, 1914	42.14	102.06	24.10
Mar. 23, 1914	35.76	96.41	21.66
Apr. 6, 1914	35.87	99.16	20.83
Apr. 24, 1914	37.22	107.22	20.28
Apr. 23, 1914	48.53	102.42	27.68
Average	40.85	......	23.57
Case 2 (Edwin T.)			
Mar. 3, 1915	43.60	86.98	29.3
Mar. 6, 1915	35.30	83.81	24.6
Mar. 10, 1915	30.94	71.57	25.8
Mar. 22, 1915	37.76	84.32	26.0
May 11, 1915	54.06	101.30	31.2
Average	40.33	......	27.3
Case 3 (J. McE.)			
Mar. 12, 1915	43.32	92.48	27.4
Mar. 31, 1915	31.59	83.55	20.17
May 14, 1915	57.31	95.75	34.9
Average	44.07	......	27.49
Case 4 (Dr. G. S. L.)			
Apr. 9, 1914	30.24	103.73	17.03
Apr. 16, 1914	36.83	102.39	20.91
Average	33.54	......	18.97
Case 5 (Peter N.), Apr. 14, 1915	28.31	74.30	12.37
Case 6 (Anna K.)			
Apr. 28, 1914	51.51	97.05	31.00
May 13, 1914	37.25	77.79	27.97
Average	44.38	......	29.48
Case 7 (Anna R.)			
May 10, 1913	31.49	62.11	29.61
May 20, 1913	43.29	71.28	18.02
May 28, 1913	41.83	67.50	36.19
May 14, 1914	29.55	68.04	25.36
Average	36.45	......	27.29
Case 8 (Sarah M.), Apr. 29, 1914	37.48	75.37	16.5
Case 9 (Marion B.), Feb. 5, 1915	35.77	80.16	26.06
Case 10 (Mrs. L.), Apr. 20, 1914	40.51	80.36	29.26
Case 11 (Bessie H.)			
Apr. 8, 1914	26.44	59.41	25.99
Apr. 13, 1914	21.06	56.81	21.65
Apr. 18, 1914	22.71	52.02	25.49
Case 12 (Benny L.)			
Apr. 10, 1914	10.48	29.61	20.67
Apr. 23, 1914	10.90	26.19	24.31
May 1, 1914	11.78	31.00	22.71
Averages Severe Cases—			
Case 1 (Max W.)	40.85	......	23.57
Case 3 (James McE.)	44.07	......	27.49
Case 4 (Dr. G. S. L.)	33.54	......	18.97
Case 6 (Anna K.)	44.38	......	29.48
Moderately Severe—			
Case 2 (Edwin T.)	40.33	......	27.3
Case 7 (Anna R.)	36.45	......	27.29
Average of six cases	39.94	......	25.7

nitrogen than the casein meal. Max W. (Case 1) showed a somewhat smaller percentage rise in metabolism than the normal controls after 100 gm. dextrose. The findings on the small cretin Benny L. (Case 12) are difficult to interpret on account of his low calorific output, but he seems to show results not far from the normal.

It appears that the specific dynamic action of protein and dextrose is approximately the same as in health. There is certainly no marked increase such as some writers[28] have surmised, and there is no marked decrease such as is found in typhoid fever. There is little difference between protein in the form of meat and in the form of casein and egg albumin.

TABLE 10.—SPECIFIC DYNAMIC ACTION OF FOODS IN HYPERTHYROIDISM

Subjects	Food	No. of Experiments	Average Gm. N or Dext. in Food	Average Gm. N or Dext. per Kg. of Body Weight	Average Gm. N or Dext. per Cal. per Hour	Average Per Cent. Rise in Metabolism above Subject's Basal
Two normal men....	Protein meal.......	2	10.1	0.149	0.144	9.7
Case 1 (Max W.).....	Casein and meat...	2	8.9	0.146	0.082	9.5
Case 2 (Edw. T.).....	Casein and meat...	2	9.6	0.19	0.12	9.0
Case 12 (Benny L.)†	Protein meal.......	1	3.6	0.15	0.135	13.0
Three normal men...	Glucose*...........	3	100.0	1.37	1.36	9.7
Case 1 (Max W.).....	....	2	100.0	1.64	0.92	5.5
Case 12 (Benny L.)†	....	1	100.0	4.20	3.7	15.0
Case 12 (Benny L.)†	....	1	70.0	2.94	2.6	7.0

* Subjects were given 115 gm. commercial glucose, which are equivalent to 100 gm. pure glucose.
† Cretin.

THE EFFECTS OF TREATMENT

Max W. (Case 1), after a stay of four months in various hospitals, was in the Bellevue metabolism ward for five days before the first determination of his basal metabolism. He received no treatment except good food, mental quiet and rest in bed with permission to get up and walk about for a few minutes at a time. In seventeen days the metabolism fell 12 per cent. After this he received the Beebe serum treatment with 1 grain of potassium iodid twice a day. In the next nineteen days the metabolism fell about 9.5 per cent., and the general condition improved correspondingly. Then while the treatment was being continued, the heat production rose almost to its level before the serum was begun. After one whole year of serum injections, during which time he was at home and at work, he returned

28. Von Noorden: New Aspects of Diabetes, New York, E. B. Treat & Co., 1912, p. 20.

to the hospital with a metabolism 5 per cent. lower than the day before treatment was begun. His mental irritability had lessened, his strength had increased, but his heart had developed fibrillation.

Edwin T. (Case 2) first took to bed when he was admitted to the metabolism ward. After a week of absolute rest in bed the first basal test was made. Three days later the metabolism was 13 per cent., and a week later 10 per cent. lower without medication. Subsequently it rose to within 4 per cent. of its original level under the influence of homesickness and some personal worries. He was given serum, but circumstances made it necessary to operate before a calorimeter test could be made. April 21, 23 and 29, all the thyroid arteries were ligated under painless local anesthesia. Twelve days after the last operation, his metabolism was 20 per cent. higher than before. He looked worse, but said he felt stronger.

James McE. (Case 3) was in the hospital twelve days before his first basal test. Immediately after this he was put on the Forcheimer ergotin and quinin hydrobromate treatment. In nineteen days the metabolism fell 5 per cent. April 10, one artery was tied; May 2, an operation was interrupted by collapse on the part of the patient. Twelve days after this the metabolism was 6 per cent. above the lowest point previously measured.

Anna K. (Case 6) was admitted to Bellevue April 27 and placed in the calorimeter the next day. On the 29th two thyroid arteries were ligated. Two weeks later the metabolism had fallen 17 per cent., which is about the decrease usually found during the first two weeks a patient is at rest in a hospital.

The basal metabolism of Anna R. (Case 7) was measured the third day she was in the hospital, May 12. On that afternoon, and May 16, the four thyroid arteries were tied. Four days later the metabolism was 15 per cent. above its original point, and eight days later it had changed but little. One year later it was at its original level.

The thyroid extract called thyroid "residue" had but slight effect on the metabolism. With Dr. G. S. L. (Case 4), a severe case, the metabolism rose slightly, with Miss B. H. (Case 11) it fell.

OBSERVATIONS ON A CRETIN

The basal metabolism of Benny L. (Case 12) averaged about 20 per cent. below the normal for adults according to his measured surface area. Children of his size average about 40 per cent. above the adult figure. This increase seems to be due chiefly to the process of growth which is lacking in the 36-year-old cretin. Although Benny's heat production is about half as great as that of a normal child of his size, we cannot consider him more than 20 per cent. below the normal for adults. The specific dynamic action of protein and carbohydrate, as we have said before, appears to be normal; but it is hard

Subject, Date, Weight, Surface Area, Linear Formula	Period	End of Period	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.
Case 1 (Max W.)..	Prelim.	11:10	.....	.....	.....	.....	.....	......	......
2/16/14 61.76 Kg. 1.72 Sq. M.	1	12:10	36.19	34.79	0.757	44.62	0.515	114.64	108.09
	2	1:10	39.28	37.60	0.760	46.04	0.515	124.08	116.54
								238.72	
Max W.	Prelim.	11:46	.....	.....	.....	.....	.....	......	......
2/18/14 62.02 Kg. 1.72 Sq. M.	1	12:46	41.81	33.14	0.917	42.53	0.658	113.45	111.71
	2	1:46	21.12	31.72	0.943	42.43	0.658	109.23	113.12
	3	2:46	38.26	33.18	0.840	42.25	0.658	111.22	114.40
								333.90	
Max W.	Prelim.	11:36	.....	.....	.....	.....	.....	......	......
2/20/14 61.60 Kg. 1.73 Sq. M.	1	12:36	32.77	31.90	0.747	40.14	0.466	104.85	102.72
	2	1:36	37.19	34.38	0.787	41.75	0.466	114.24	105.67
								219.09	
Max W.	Prelim.	10:45	.....	.....	.....	.....	.....	......	......
2/21/14 62.26 Kg. 1.73 Sq. M.	1	11:45	43.56	35.33	0.897	40.98	0.456	120.82	112.67
	2	12:45	45.07	33.52	0.978	41.85	0.456	117.20	116.41
								238.02	
Max W.	Prelim.	11:32	.....	.....	.....	.....	.....	......	......
2/25/14 61.18 Kg. 1.71 Sq. M.	1	12:32	41.19	36.32	0.825	39.85	0.317	121.27	114.35
	2	1:32	43.37	37.60	0.839	41.29	0.317	126.06	123.58
								247.33	
Max W.	Prelim.	11:18	.....	.....	.....	.....	.....	......	......
2/27/14 60.86 Kg. 1.70 Sq. M.	1	12:18	35.58	33.18	0.781	41.05	0.650	109.55	112.07
	2	1:18	35.94	34.25	0.763	41.90	0.650	112.78	112.12
								222.33	
Max W.	Prelim.	11:50	.....	.....	.....	.....	.....	......	......
3/2/14 60.47 Kg. 1.70 Sq. M.	1	12:50	37.25	35.42	0.765	45.44	0.668	116.70	112.28
	2	1:50	38.75	32.28	0.873	46.48	0.668	109.25	112.08
								225.95	
Max W.	Prelim.	10:52	.....	.....	.....	.....	.....	......	......
3/4/14 60.02 Kg. 1.70 Sq. M.	1	11:52	31.79	30.79	0.751	39.10	0.550	101.10	105.05
	2	12:52	34.55	32.04	0.784	45.17	0.550	106.19	111.50
								207.29	
Max W.	Prelim.	11:06	.....	.....	.....	.....	.....	......	......
3/28/14 59.20 Kg. 1.68 Sq. M.	1	12:06	28.32	27.13	0.759	34.87	0.319	89.59	98.12
	2	1:06	29.31	27.63	0.771	34.44	0.319	91.46	97.22
	3	2:06	31.76	29.39	0.786	37.98	0.319	97.79	96.40
								278.84	

—Calorimetry in Goiter

Direct Calorimetry (Rectal Temp.), Cal.	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M. (Meeh)	
......	37.41	...	....	.....	..	..	..	....	.....	Basal
103.52	37.33	131	31.4	0.750	12	75	13	1.85	59.58	Restless
125.28	37.51	142	14.6	0.754	11	75	14	2.01	64.49	Restless
228.80										
......	37.04	...	....	.....	..	..	..	....	.....	Dextrose in lemonade, 100 gm. at 10:55-11:00
103.40	36.89	127	20.0	0.940	15	17	68	1.83	58.78	
110.83	36.87	123	20.8	0.972	16	8	76	1.76	56.60	
115.92	36.84	123	31.2	0.847	16	44	40	1.80	57.63	
330.15										
......	36.96	...	....	.....	..	..	..	....	.....	Basal
87.44	36.67	103	16.0	0.789	12	78	10	1.70	54.58	Quiet
123.60	37.03	114	21.5	0.784	11	65	24	1.85	59.47	Quiet
211.04										
......	36.76	...	....	.....	..	..	..	....	.....	Dextrose in lemonade, 100 gm. at 9:55-9:57
108.59	36.69	108	25.7	0.908	10	28	62	1.94	62.47	Quiet
117.48	36.72	107	60.0	0.997	10	1	89	1.88	60.60	Restless
226.07										
......	37.44	...	....	.....	..	..	..	....	.....	Protein meal; N = 8.9 gm. at 10 a. m.
111.31	37.39	139	19.6	0.829	18	48	34	1.98	63.46	Quieter
129.64	37.52	137	33.0	0.846	17	44	39	2.06	65.97	Quieter
240.95										
......	37.12	...	....	.....	..	..	..	....	.....	Basal
105.53	37.00	137	47.6	0.776	16	64	20	1.80	57.51	Restless
113.14	37.01	135	56.0	0.755	15	71	14	1.85	59.20	Restless
218.67										
......	37.03	...	....	.....	..	..	..	....	.....	Protein meal; N = 9.0 gm. at 10:04 a. m.
112.64	37.10	98	35.6	0.757	15	70	15	1.93	61.52	Asleep 15 min.
119.50	37.26	103	41.2	0.887	16	32	52	1.81	57.59	Quiet
232.14										
......	37.12	...	....	.....	..	..	..	....	.....	Basal
93.60	36.90	99	15.3	0.741	14	76	10	1.68	53.55	Asleep all the hour
110.52	36.89	116	58.0	0.781	14	64	22	1.77	56.24	Awake
204.12										
......	36.94	...	....	.....	..	..	..	....	.....	Basal
92.25	36.83	88	15.2	0.754	9	76	15	1.51	47.91	Asleep 45 min.
95.27	36.80	87	24.1	0.768	9	72	19	1.55	48.91	Asleep 24 min.
101.70	36.92	85	25.4	0.784	9	67	24	1.65	52.29	Fairly quiet
289.22										

TABLE 11.—

Subject, Date, Weight, Surface Area, Linear Formula	Period	End of Period	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.
Max W.	Prelim.	11:15	.....	.....	.....	.....	.....	......	......
4/6/14 61.32 Kg. 1.71 Sq. M.	1	12:15	30.11	27.75	0.789	30.36	0.402	92.23	91.14
	2	1:15	32.13	29.98	0.779	35.74	0.402	99.44	99.65
	3	2:15	33.39	30.43	0.798	40.02	0.402	101.44	102.02
								293.11	
Max W.	Prelim.	11:13	.....	.....	.....	.....	.....	......	......
4/24/14 63.35 Kg. 1.75 Sq. M.	1	12:13	33.83	31.77	0.774	34.51	0.554	105.02	97.07
	2	1:13	35.04	32.60	0.782	39.98	0.554	108.00	106.82
								213.02	
Max W.	Prelim.	11:12	.....	.....	.....	.....	.....	......	......
4/23/15 73.27 Kg. 1.854 Sq. M.	1	12:12	32.82	31.30	0.763	45.09	0.669	102.84	103.95
	2	1:12	35.71	33.68	0.771	51.97	0.669	110.98	113.02
								213.82	
Case 2 (Edw. T.)..	Prelim.	11:06	.....	.....	.....	.....	.....	......	......
3/3/15 49.75 Kg. 1.475 Sq. M.	1	12:06	29.78	.....	.....	40.78	0.506	......	87.99
	2	1:06	30.48	28.26	0.785	43.55	0.506	93.59	94.69
	3	2:36	42.85	40.61	0.767	68.26	0.506	133.87	134.88
								227.46	
Edw. T.	Prelim.	11:00	.....	.....	.....	.....	.....	......	......
3/5/15 50.39 Kg. 1.483 Sq. M.	1	12:00	31.68	25.98	0.887	47.66	0.913	87.46	92.27
	2	1:00	33.04	27.48	0.874	46.16	0.913	92.31	96.99
	3	2:00	31.61	26.99	0.852	45.40	0.849	90.32	98.20
	4	3:00	29.97	26.74	0.815	45.94	0.849	88.62	95.06
								358.71	
Edw. T.	Prelim.	10.44	.....	.....	.....	.....	.....	......	......
3/6/15 50.00 Kg. 1.478 Sq. M.	1	11.44	27.56	23.99	0.836	36.38	0.583	80.18	84.34
	2	12:43	25.72	23.88	0.783	33.64	0.573	78.84	77.52
								159.02	
Edw. T.	Prelim.	11:02	.....	.....	.....	.....	.....	......	......
3/8/14 49.69 Kg. 1.474 Sq. M.	1	12:02	30.74	27.57	0.811	45.28	0.966	91.02	95.40
	2	1:02	32.81	29.73	0.803	43.97	1.006	98.11	98.78
	3	2:02	31.85	27.44	0.844	40.31	1.006	91.32	91.73
								280.45	
Edw. T.	Prelim.	10:56	.....	.....	.....	.....	.....	......	......
3/10/15 49.32 Kg. 1.47 Sq. M.	1	11:56	24.59	22.82	0.784	29.58	0.541	75.36	79.29
	2	12:56	29.05	26.22	0.806	32.30	0.541	87.29	88.84
								162.65	

—(*Continued*)

Direct Calorimetry (Rectal Temp.), Cal.	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M. (Meeh)	
......	36.68	...	....	.....	..	..	..	....	.....	Basal
86.09	36.59	93	25.4	0.787	12	64	24	1.51	48.16	Asleep 50 min.
103.27	36.67	90	55.0	0.776	11	68	21	1.62	51.98	Very restless
108.13	36.80	102	67.0	0.797	10	62	28	1.65	52.97	Very restless
297.47										
......	36.68	...	....	.....	..	..	..	....	.....	Basal
100.23	36.75	125	40.5	0.769	14	68	18	1.66	53.66	
114.21	36.90	115	57.0	0.778	14	65	21	1.71	55.19	
214.44										
......	37.04	...	....	.....	..	..	..	....	.....	Basal
93.62	36.87	101	21.0	0.758	17	70	13	1.40	47.70	Asleep 30 min.; quiet
111.22	36.85	97	33.0	0.764	16	69	15	1.52	51.48	Asleep 5 min.; quiet
204.84										
......	37.72	...	....	.....	..	..	..	....	.....	Basal
85.15	37.66	99	35.0	.....	..	..	..	....	.....	Restless
88.14	37.51	98	23.0	0.781	14	64	22	1.86	56.21	Reading 45 min.
131.13	37.45	99	46.0	0.768	10	73	17	1.79	53.61	Asleep 50 min.
219.27										
......	37.93	...	....	.....	..	..	..	....	.....	Protein meal*
77.14	37.56	90	6.0	0.922	28	20	52	1.74	52.06	Asleep 60 min.
80.52	37.20	87	14.0	0.902	26	25	49	1.83	54.95	Reading 52 min.
94.40	37.29	86	19.0	0.869	25	33	42	1.79	53.76	Quiet
93.40	37.32	88	15.0	0.819	25	46	29	1.76	52.75	Reading 30 min.; quiet 30 min.
345.46										
......	37.25	...	....	.....	..	..	..	....	.....	Basal
81.35	37.19	85	6.0	0.844	19	44	37	1.60	47.98	Reading 60 min.; very quiet
84.89	37.38	88	18.0	0.778	19	60	21	1.58	47.11	Asleep 55 min.; fairly quiet
166.24										
......	37.98	...	....	.....	..	..	..	....	.....	Meat; 10.19 gm. N at 8:55-9:04
88.69	37.78	93	19.0	0.814	28	46	26	1.83	54.70	Asleep 60 min.
85.37	37.47	95	5.0	0.802	26	50	24	1.97	58.96	Reading 60 min.
88.96	37.46	97	42.0	0.862	29	34	37	1.84	54.88	Awake, restless
263.02										
......	37.87	...	....	.....	..	..	..	....	.....	Basal
69.79	37.65	89	16.0	0.789	16	60	24	1.58	45.51	Asleep, slightly restless
73.34	37.28	95	18.0	0.777	14	64	22	1.77	52.71	Reading 55 min.
143.13										

* Protein = 56.0 gm. (Nitro. = 8.95 gm.); Fat = 8.5 gm.; Carbh. = 47.1 gm.; 8:55 to 9:32 a. m.

TABLE 11.—

Subject, Date, Weight, Surface Area, Linear Formula	Period	End of Period	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.
Edw. T.	Prelim.	11:07	.....	.....	.....	.....	.....	......	......
3/22/15 49.17 Kg. 1.468 Sq. M.	1	12:07	25.80	23.71	0.791	35.67	0.348	78.86	82.01
	2	1:07	29.12	26.38	0.803	35.17	0.348	88.01	87.01
	3	2:07	30.48	28.59	0.775	42.45	0.348	94.78	92.51
								261.65	
Edw. T.	Prelim.	11:33	.....	.....	.....	.....	.....	......	......
5/11/15 50.37 Kg. 1.483 Sq. M.	1	12:33	31.02	28.27	0.798	48.24	0.452	96.16	95.55
	2	1:33	33.75	34.47	0.712	59.87	0.452	115.11	107.61
								211.27	
Edw. T.	Prelim.	11:35	.....	.....	.....	.....	.....	......	......
11/1/15 52.68 Kg. 1.508 Sq. M.	1	12:35	31.77	29.39	0.786	53.39	0.358	97.73	95.07
	2	1:35	33.17	30.60	0.789	51.38	0.358	101.89	95.48
Case 3 (Jas. McE.)	Prelim.	11:16	.....	.....	.....	.....	.....	......	......
3/12/15 41.16 Kg. 1.319 Sq. M.	1	12:16	31.34	28.78	0.792	40.88	0.398	95.77	91.74
	2	1:16	30.92	29.96	0.751	45.31	0.398	98.57	96.66
	3	1:46	16.67	15.27	0.794	22.09	0.398	50.84	48.20
								245.18	
James McE.	Prelim.	11:00	.....	.....	.....	.....	.....	......	......
3/31/15 39.98 Kg 1.303 Sq. M.	1	12:00	30.55	26.24	0.846	29.79	0.316	88.61	80.65
	2	1:00	31.49	28.62	0.800	33.38	0.316	95.60	86.04
								184.21	
James McE.	Prelim.	11:12	.....	.....	.....	.....	.....	......	......
5/14/15 45.29 Kg. 1.371 Sq. M.	1	12:12	32.14	31.91	0.732	55.70	0.301	104.91	96.97
	2	1:12	33.34	31.25	0.776	58.92	0.301	103.73	101.66
								208.64	
Case 4 (Dr.G.S.L.)	Prelim.	11:08	.....	.....	.....	.....	.....	......	......
4/9/14 71.78 Kg. 1.89 Sq. M.	1	12:08	33.19	31.92	0.756	30.25	0.398	105.33	105.66
	2	1:08	33.30	30.88	0.784	30.23	0.398	102.62	102.22
								207.95	
Dr. G. S. L.	Prelim.	11:20	.....	.....	.....	.....	.....	......	......
4/16/14 69.40 Kg. 1.86 Sq. M.	1	12:20	32.58	31.94	0.742	35.50	0.460	104.83	106.58
	2	1:20	34.95	33.05	0.769	33.16	0.460	109.29	102.25
								214.12	
Case 5 (Peter N.)..	Prelim.	11:23	.....	.....	.....	.....	.....	......	......
4/14/15 63.44 Kg. 1.795 Sq. M.	1	12:23	22.85	20.32	0.818	23.42	0.375	67.89	77.85
	2	1:23	24.71	21.14	0.850	23.19	0.375	71.28	76.70
								139.17	

—(*Continued*)

Direct Calorimetry (Rectal Temp.), Cal.	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M. (Meeh)	
......	37.11	...	....	.....	..	..	..	....	.....	Basal
76.63	36.99	100	....	0.790	12	63	25	1.60	47.71	Sleeping, very quiet
80.53	36.83	108	10.0	0.808	10	61	29	1.79	54.48	Reading, quiet
97.31	36.97	112	30.0	0.772	10	70	20	1.73	57.34	Sleeping
254.47										
......	37.23	...	....	.....	..	..	..	....	.....	Basal after ligation
95.83	37.25	131	15.0	0.772	12	69	19	1.91	57.31	Restless
106.76	37.24	137	34.0	0.688	10	90	0	2.29	68.60	Restless
202.59										
......	37.16	...	....	.....	..	..	..	....	.....	Basal 6 mos. after ligation
90.04	37.06	96	13.0	0.786	10	66	24	1.86	56.5	Quiet; sleeping
100.06	37.18	107	14.0	0.789	9	65	26	1.94	58.9	Quiet; awake
......	38.26	...	....	.....	..	..	..	....	.....	Basal
87.48	38.15	106	14.0	0.790	11	64	25	2.33	65.24	Quiet; reading
92.07	38.08	110	23.0	0.744	11	79	10	2.40	67.15	Quiet; reading
51.66	38.21	114	15.0	0.793	10	64	26	2.47	69.26	Fairly quiet
231.21										
......	36.88	...	....	.....	..	..	..	....	.....	Basal after quinin and ergotin
82.62	36.90	95	10.0	0.851	9	46	45	2.22	61.54	Quiet; reading
94.47	37.21	99	26.0	0.800	9	62	29	2.39	66.39	Reading 32 min.; restless 28 min.
177.09										
......	37.20	...	....	.....	..	..	..	....	.....	Basal after ligation
89.64	37.02	111	14.0	0.726	8	85	7	2.32	68.61	Fairly quiet
101.86	37.04	119	7.0	0.778	8	72	20	2.29	67.81	Fairly quiet
191.50										
......	36.57	...	..	.....	..	..	..	....	.....	Basal
104.54	36.56	98	24	0.751	10	76	14	1.47	49.54	Quiet
102.91	36.58	101	16	0.782	10	67	23	1.48	48.27	Quiet
207.45										
......	36.88	...	..	.....	..	..	..	....	.....	Basal; at 9:35-9:50 a. m. 1.0 c.c. thyroid "residue"
101.60	36.80	97	29	0.733						
104.17	36.84	101	58	.0764	12	80	8	1.51	50.42	Fairly quiet
205.77					11	71	18	1.57	52.57	Restless
......	37.27	...	..	.....						
73.79	37.15	71	6	0.820	..	..	..	....	.....	Basal
75.80	37.13	71	2	0.858	15	52	33	1.07	34.66	Very quiet
149.59					14	41	45	1.12	36.39	Very quiet

Subject, Date, Weight, Surface Area, Linear Formula	Period	End of Period	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.
Case 6 (Anna K.)..	Prelim.	11:12	.....	.....	.....	.....	.....	......	......
4/28/14 44.45 Kg.	1	12:12	31.78	31.25	0.738	49.35	0.407	102.57	97.70
	2	1:12	32.00	30.79	0.756	53.67	0.407	101.53	100.83
								204.10	
Anna K.	Prelim.	11:40	.....	.....	.....	.....	.....	......	......
5/13/14 44.50 Kg.	1	12:40	27.62	24.63	0.816	33.43	0.505	82.14	69.53
	2	1:40	28.40	26.01	0.794	41.06	0.505	86.31	81.27
								168.45	
Case 7 (Anna R.)..	Prelim.	9:45	.....	.....	.....	.....	.....	......	......
5/10/13 46.71 Kg.	1	10:45	22.05	21.02	0.763	29.44	0.287	69.42	61.67
	2	11:45	21.67	17.95	0.878	29.64	0.287	60.98	60.15
	3	12:45	22.55	22.15	0.740	35.40	0.287	72.74	65.27
								203.14	
Anna R.	Prelim.	9:30	.....	.....	.....	.....	.....	......	......
5/20/13 42.91 Kg.	1	10:30	23.74	21.93	0.787	36.63	0.380	72.73	65.30
	2	11:30	24.72	23.55	0.763	43.42	0.380	77.68	72.33
	3	12:30	24.16	24.52	0.717	49.32	0.380	80.01	83.34
								230.41	
Anna R.	Prelim.	9:38	.....	.....	.....	.....	.....	......	......
5/28/13 43.29 Kg.	1	10:38	23.15	22.21	0.758	42.19	0.423	73.04	71.31
	2	11:38	22.13	21.01	0.766	38.89	0.423	69.19	67.38
	3	12:38	23.19	21.29	0.792	44.42	0.423	70.60	74.19
								212.83	
Anna R.	Prelim.	11:13	.....	.....	.....	.....	.....	......	.....
5/14/14 43.20 Kg.	1	12:13	22.79	20.90	0.793	29.00	0.282	69.58	59.76
	2	1:13	23.55	21.86	0.784	30.09	0.282	72.63	65.43
								142.21	
Case 8 (Sarah M.)	Prelim.	11:20	.....	.....	.....	.....	.....	......	.....
4/29/14 55.96 Kg.	1	12:20	25.62	23.85	0.781	37.36	0.363	79.07	76.95
	2	1:20	25.28	23.79	0.773	37.09	0.363	78.70	79.67
								157.77	
Case 9 (Marion B.)	Prelim.	11:35	.....	.....	.....	.....	.....	......	.....
2/5/15 57.91 Kg.	1	12:35	25.89	25.26	0.746	35.16	0.195	83.30	80.18
	2	1:35	25.80	23.59	0.796	35.15	0.195	78.91	79.99
	3	2:35	26.10	24.44	0.775	37.01	0.195	81.35	86.23
								243.56	
Case 10 (Mrs. L.)..	Prelim.	11:18	.....	.....	.....	.....	.....	......	.....
4/20/14 63.00 Kg.	1	12:18	25.45	25.30	0.732	40.91	0.382	82.79	85.12
	2	1:18	26.64	24.35	0.795	40.10	0.382	81.00	84.18
								163.79	

—(*Continued*)

Direct Calorimetry (Rectal Temp.), Cal.	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M. (Meeh)	
......	37.18	...	..	.....						
95.12	37.12	118	36	0.730	..	..	..	....	.....	Basal
98.98	37.08	128	38	0.750	11	82	7	2.31	66.39	Restless
194.10					11	76	13	2.23	65.71	Quiet
......	37.04	...	..	.....						
71.74	37.11	95	10	0.818	..	..	..	....	.....	Basal
83.84	37.19	105	13	0.792	16	52	32	1.85	54.37	Very quiet
155.58					16	59	25	1.94	55.83	Very quiet
......	37.39	119	..	.....						
59.36	37.34	...	30	0.758	..	..	..	....	.....	Basal
61.31	37.38	...	14	0.890	11	73	16	1.49	44.50	
65.65	37.40	...	36	0.783	12	33	55	1.31	39.09	
186.32					10	82	8	1.56	46.63	
......	37.37	...	..	.....						
65.02	37.99	...	8	0.784	..	..	..	....	.....	Basal
67.81	37.98	...	12	0.757	14	63	23	1.69	48.23	Quiet
81.02	38.04	...	11	0.708	13	72	15	1.81	51.51	Quiet
213.85					13	87	0	1.86	53.06	Quiet
......	37.16	...	..	.....						
66.87	37.16	...	..	0.749	..	..	..	....	.....	Basal
65.89	37.23	...	..	0.758	15	73	12	1.69	49.99	
69.74	37.23	...	..	0.789	16	69	15	1.60	47.36	
202.50					16	60	24	1.63	48.32	
......	36.69	...	..	.....	..	..	..	....	.....	Basal 1 yr. later
67.01	36.88	97	9	0.791	11	63	26	1.44	42.69	Very quiet; dozed
69.07	36.98	97	10	0.781	10	67	23	1.51	44.56	Very quiet; dozed
136.08										
......	37.33	...	..	.....	..	..	..	....	.....	Breakfast at 7 a. m.; toast 20 gm., milk 250 c.c.
73.30	37.26	97	24	0.778	12	66	22	1.41	43.90	Fairly quiet
77.44	37.22	86	33	0.768	12	69	19	1.40	43.70	Fairly quiet
150.74										
......	37.00	...	..	.....	..	..	..	....	.....	Basal
73.61	36.87	114	46	0.742	6	83	11	1.44	45.20	Restless
82.04	36.92	132	31	0.795	7	63	30	1.36	42.82	Restless
84.82	36.91	136	36	0.773	6	73	21	1.41	44.14	Reading
240.47										
......	38.18	...	..	.....	..	..	..	....	.....	Basal
81.05	38.11	81	26	0.721	12	84	4	1.31	42.46	Restless
80.67	38.05	88	36	0.794	12	62	26	1.29	41.54	Restless
161.72										

TABLE 11.—

Subject, Date, Weight, Surface Area, Linear Formula	Period	End of Period	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.
Case 11 (Bessie H.)	Prelim.	11:40	.....	.....	.....	.....	.....	......	.....
4/8/14 47.06 Kg. 1.42 Sq. M.	1	12:40	19.06	17.02	0.815	26.67	0.159	57.12	62.51
	2	1:40	19.41	16.68	0.846	26.21	0.159	56.44	61.34
								113.56	
Bessie H.	Prelim.	11:27	.....	.....	.....	.....	.....	......	.....
4/13/14 48.13 Kg. 1.43 Sq. M.	1	12:27	18.42	16.22	0.826	20.81	0.125	54.63	56.23
	2	1:27	19.49	17.83	0.795	21.81	0.125	59.60	59.33
								114.23	
Bessie H.	Prelim.	11:05	.....	.....	.....	.....	.....	......	.....
4/18/14 46.62 Kg. 1.41 Sq. M.	1	12:05	17.83	15.14	0.856	22.12	0.217	51.02	52.61
	2	1:05	18.57	16.57	0.815	23.29	0.217	55.49	54.37
								106.51	
Case 12 (Benny L.)	Prelim.	11:40	.....	.....	.....	.....	.....	......	.....
4/10/14 22.80 Kg. 0.829 Sq. M.	1	12:40	10.28	7.67	0.974	10.45	0.363	26.10	31.38
	2	1:40	10.23	8.58	0.867	10.51	0.363	28.68	32.70
								54.78	
Benny L.	Prelim.	11.52	.....	.....	.....	.....	.....	......	.....
4/14/14 23.60 Kg. 0.84 Sq. M.	1	12:52	13.13	9.40	1.016	12.54	0.293	32.58	32.32
	2	1:52	12.81	9.24	1.008	12.29	0.293	31.97	33.39
	3	2:52	12.05	8.99	0.975	11.69	0.293	30.91	33.32
								95.46	
Benny L.	Prelim.	11:10	.....	.....	.....	.....	.....	......	.....
4/21/14 24.04 Kg. 0.847 Sq. M.	1	12:10	11.23	8 10	1.008	13.82	0.316	27.91	33.30
	2	1:10	11.02	8.90	0.899	13.47	0.316	30.18	32.12
	3	2:10	11.07	9.04	0.890	13.21	0.316	30.43	33.95
	4	3:10	11.15	8.79	0.923	12.94	0.316	29.86	33.30
								118.38	
Benny L.	Prelim.	11:10	.....	.....	.....	.....	.....	......	.....
4/23/14 23.97 Kg. 0.847 Sq. M.	1	12:10	9.44	7.76	0.885	10.58	0.226	26.21	26.47
	2	1:10	9.20	7.83	0.855	11.21	0.226	26.25	28.57
								52.46	
Benny L.	Prelim.	11:20	.....	.....	.....	.....	.....	......	.....
4/27/14 23.86 Kg. 0.847 Sq. M.	1	12:20	10.47	7.94	0.959	14.30	0.208	27.36	27.15
	2	1:20	10.75	8.33	0.939	13.79	0.208	28.58	29.55
	3	2:20	11.01	8.38	0.955	13.29	0.208	28.88	29.25
								84.82	
Benny L.	Prelim.	11:10	.....	.....	.....	.....	.....	......	.....
5/1/14 23.08 Kg. 0.833 Sq. M.	1	12:10	10.86	10.05	0.785	11.67	0.236	33.22	31.09
	2	1:12	10.91	9.96	0.797	11.88	0.236	32.99	31.80
								66.21	

—(*Continued*)

Direct Calorimetry (Rectal Temp.), Cal.	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M. (Meeh)	
......	37.22	...	..	.....	..	..	..	....	.....	Basal
55.89	37.06	60	4	0.815	7	59	34	1.22	35.59	Quiet
62.93	37.11	59	3	0.850	7	47	46	1.20	35.17	Quiet
118.82										
......	37.15	...	..	.....	..	..	..	....	.....	Basal
51.06	37.03	72	3	0.828	6	55	39	1.18	33.52	Very quiet
62.55	37.12	75	13	0.795	6	66	28	1.24	36.56	Very quiet
113.61										
......	37.19	...	..	.....	..	..	..	....	.....	Basal; 1.0 c.c. thyroid "residue" at 9:30 a. m.
51.86	37.18	93	3	0.847	11	46	43	1.10	31.99	Very quiet
52.18	37.12	90	15	0.816	10	56	34	1.19	34.79	Very quiet
104.04										
......	37.51	...	..	.....	..	..	..	....	.....	Basal
28.47	37.37	83	2	1.089	37	0	63	1.15	26.36	Very quiet
30.74	37.28	85	2	0.908	34	12	44	1.26	28.92	Very quiet
59.21										
......	37.59	..	..	.....	..	..	..	....	.....	Lactose 100 gm.; water and lemon juice, 200 c.c.
30.10	37.49	89	2	1.092	24	0	76	1.38	32.16	Very quiet
32.56	37.46	89	2	1.063	24	0	76	1.35	31.56	Very quiet
31.62	37.36	87	2	1.040	25	0	75	1.31	30.51	Very quiet
94.28										
......	37.41	..	..	.....	..	..	..	....	.....	Protein meal at 9:38-9:55 a. m.; N = 3.6 gm.
31.46	37.33	87	6	1.109	30	0	70	1.16	27.20	Very quiet
31.07	37.29	81	5	0.989	28	15	57	1.25	29.87	Very quiet
32.50	37.23	81	9	0.927	27	18	55	1.27	29.71	Quiet
31.46	37.15	78	10	0.974	28	6	66	1.24	29.10	Quiet
126.49										
......	37.16	..	..	.....	..	..	..	....	.....	Basal
25.44	37.12	79	5	0.911	23	23	54	1.09	25.60	Very quiet
26.93	37.05	77	9	0.871	23	34	43	1.09	25.63	Quiet
52.37										
......	37.34	..	..	.....	..	..	..	....	.....	Dextrose, 70 gm. at 10:20 - 10:22 a. m.
26.52	37.32	78	3	1.004	20	0	80	1.15	26.82	Very quiet
28.92	37.30	79	4	0.975	19	7	74	1.20	28.02	Very quiet
29.41	37.32	80	5	0.996	19	1	80	1.21	28.31	Very quiet
84.85										
......	37.76	..	..	.....	..	..	..	....	.....	Thyroid extract
30.07	37.72	94	3	0.781	19	60	21	1.44	33.33	Very quiet
31.92	37.74	95	4	0.795	19	56	25	1.43	33.10	Very quiet
61.99										

to find the proper basis on which to compare it with results obtained on normal adults. The administration of thyroid extract raised the metabolism to normal in three and a half days, increased the pulse rate from about 80 to 95, and made the patient sick and miserable.

THERAPEUTIC APPLICATIONS

Mental and physical rest is the surest means of securing the drop in the metabolism which indicates a diminution in the pernicious activity of the thyroid. Psychotherapy is of some value, and this combined with rest may account entirely for the improvement following most of the so-called medical cures. Previous observers have found little or no reduction in the oxidative processes after treatment with "Radogen," the serum of thyroidectomized horses, and the Roentgen ray. To this list may be added from the present work thyroid "residue," the ergotin and quinin hydrobromate treatment, and Beebe's serum. These remedies, however, were tried on but one or two patients, and a more favorable report might have been justified if more cases had been tested. In the treatment of hyperthyroidism, calorimeters and other forms of respiratory apparatus seem to be therapeutic nihilists.

Some observers have found a prompt drop in the metabolism after a partial thyroidectomy. Ligation of the arteries usually causes a distinct rise in heat production which may last several weeks. This shows that following a ligation of the arteries the patients should be kept as quiet as possible and thyroid extract should on no account be given.

It is quite possible that the above mentioned therapeutic agents control some of the minor symptoms of the disease or render the major symptoms less apparent to the patient and his physician. We cannot consider the patient to be anywhere near a cure until the metabolism has approached the normal. We cannot consider a therapeutic agent to be curative unless it causes the metabolism to approach the normal more quickly than the tendency toward spontaneous improvement aided by mental and physical rest.

The need of large amounts of food by exophthalmic goiter patients is clearly shown. There is no indication against the use of fairly liberal amounts of protein, and there is no reason to prefer the proteins of vegetables and milk to those of meat. The number of calories required per day varies with the weight of the patient, the severity of the case and the degree of muscular activity. In general, it may be said that exophthalmic goiter patients need from one and one-half times to twice as much food as a normal person under similar conditions. Several of the patients studied produced over 100 calories an hour while at rest. Max W. (Case 1) and Edwin T. (Case 2) showed a slightly negative nitrogen balance when receiving 3,500 and

4,000 calories a day. Every effort should be made to give food of high caloric value in large amounts, or there will be losses of body fat and protein.

SUMMARY AND CONCLUSIONS

The metabolism in exopthalmic goiter has been studied for the first time in a respiration apparatus which is also a calorimeter. Thirty-seven observations were made on eleven patients with this disease, and six experiments were made on a cretin. With some of the patients the nitrogen balance was also studied.

The measurement of the heat production gives us the best index of the severity of the disease and of the effect of treatment. Very severe cases show an increase of 75 per cent. or more above the normal average, severe cases 50 per cent. or more, and moderately severe and mild cases less than 50 per cent., while a few mild and several atypical or cases in which operation has been performed may be within normal limits. In severe cases the warmth of skin and sweating can be accounted for entirely by the necessity for the increased elimination of heat. At least a part of the tachycardia is due to the increased metabolism, and perhaps it might be possible to reproduce the extreme tachycardia, the cardiac enlargement, emaciation and mental irritability if we were able to stimulate the metabolism of normal men for twenty-four hours a day over a period of months or years.

The specific dynamic action of protein and of glucose is within normal limits, and there is no consistent difference between the effects of protein in meat and an equal amount in milk and eggs. One patient was able to derive 89 per cent. of his calories from carbohydrate in an experiment when he was showing an alimentary glycosuria. There is evidently no interference with the oxidation of carbohydrates.

The methods of direct and indirect calorimetry agree very closely when one considers the technical difficulties. The method of direct calorimetry gave results which were slightly lower than the indirect, the total difference being 2.9 per cent., and the average difference in the individual experiments being $\pm$ 4.1 per cent. This and the absence of abnormal respiratory quotients shows that the law of the conservation of energy holds good in exophthalmic goiter, and that there is no profound disturbance of the intermediary metabolism.

The average water elimination through skin and lungs in the severe and moderately severe cases of hyperthyroidism is 39.9 gm. per hour. The increase above the normal is closely proportional to the increase in heat production; 25.7 per cent. of the calories are dissipated through vaporization in goiter patients, whereas the mean normal is almost the same, 23.9 per cent.

The level of the heat production was used as an index of the effect of medical treatment. Rest in bed for a week or more caused a drop of more than 10 per cent. The effects of treatment with Beebe's serum, thyroid "residue" ergotin and quinin hydrobromate was less marked each being tested on one patient. Ligation of the thyroid arteries with three out of the four patients studied caused a distinct rise in metabolism, the duration of which was uncertain. There is as yet no proof that any conservative form of treatment causes a greater reduction of metabolism than mental and physical rest.

One small cretin 36 years old produced about half the calories eliminated by children of his size. As estimated by the surface area, his metabolism was about 20 per cent. below the normal adult level. Three and a half days of treatment with thyroid extract raised his heat production to normal.

Note.—The work here reported was made possible by the cooperation of a number of associates who should receive credit for the major part of the work. The analyses of food, urine and feces were made by Mr. Frank C. Gephart, with the assistance of Mr. R. H. Harries and Mr. R. C. Stone. The electrical control of the calorimeter was in charge of Mr. G. F. Soderstrom, and the residual air analyses and calculations were made by Dr. A. L. Meyer and Mr. Harries. The results were checked and tabulated by Miss Grace Sims and Mr. Stone. Miss Estelle Magill and her assistants, Miss A. Honold, Miss M. M. Fauquier and others were responsible for the weighing and preparation of the food, the care of the patients and the collection of specimens.

I wish to express my thanks to Dr. John Rogers for providing most of the patients and for cooperating very actively in the work. I also wish to thank Dr. S. P. Beebe for supervising the serum treatment and Dr. G. R. Lockwood of the First Medical Division of Bellevue for permitting the use of material from his ward, and to Drs. W. H. Brundage, T. C. Janeway and R. J. Shea, who also sent patients for treatment and observation.

CLINICAL CALORIMETRY

FIFTEENTH PAPER

THE BASAL METABOLISM IN PERNICIOUS ANEMIA *

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HISTORICAL

The view that a paucity of hemoglobin must seriously impair the oxidative processes of the body received dogmatic credence for many years. Although based on *a priori* considerations, it was apparently supported by animal experimentation, chiefly that of Bauer.[1] In Bauer's experiments the effect of hemorrhage is difficult of ascertainment. Food, fasting and the mechanical effect of blood loss are disturbing factors. The vomiting of Bauer's dog leads one to suspect that the animal was unfit for the purpose in hand.

At any rate, subsequent investigation on animals failed to substantiate any pronounced fall in the metabolic functions of the body in anemia. The observations of Finkler,[2] Lukjanow,[3] Pembrey[4] and

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1. Baur: Ueber die Zersetzungsvorgänge im Thierkörper unter dem Einfluss von Blutenziehungen, Ztschr. f. Biol., 1872, viii, 567.

2. Finkler Ueber den Einfluss der Strömungsgechwindichkeit und Menge des Blutes auf die tierische Verbrennung. Arch. f. d. ges. Physiol. (Pflüger's), 1875, x, 368.

3. Lukjanow: Ueber die Aufnahme von Sauerstoff bei Erhöhthem Procentegehalt desselben in der Luft, Ztschr. f. Phys. Chem., 1883, viii, 315.

4. Pembrey: Influence of Bleeding and Transfusion on Respiratory Exchange, Jour. Physiol., 1895, xv, 449.

Gürber and Delchef[5] effected a modification of the current hypothesis, inasmuch as no permanent departure from the normal metabolism could be found. There are variations, to be sure, but the tendency is distinctly toward normality. The slight increase in heat production which Fredericq[6] measured with the d'Arsonval compensation calorimeter is well within the limits of the experimental error. Only once did Hari,[7] working in Tangl's laboratory with a Rubner calorimeter, find an increase of 12 per cent. in the heat production of a dog.

The anemias in animals have been artificially induced by blood-letting. It is open to question whether the anemias studied in animals are at all comparable with those obtaining in the clinic. When we come to the application of experimental methods to clinical anemia, the problem at once becomes decidedly more complicated. In addition to the simple anemias, there is the unique type of pernicious anemia. Chlorosis and leukemia may be included in the category because of their low hemoglobin content. Any difference that the clinical forms show may, quite apart from refinement of technic, be ascribed to essential differences between anemias artificially induced and anemias arising from pathologic agencies.

Magnus-Levy[8] points out that Pettenkofer and Voit's pioneer experiment on a leukemic man, if properly interpreted, actually reveals an increase in the metabolism.

Both Kraus[9] and Bohland[10] find the metabolism near the upper physiologic limits, and that in some cases (Bohland) it may really exceed these limits. Thiele and Nehring,[11] while observing a slight increase in secondary anemia, could not establish a diminution in the oxygen intake in chlorotics. In the hands of Magnus-Levy,[12] pernicious anemia yields a metabolism somewhat elevated. Grafe[13] finds

5. Gürber and Delchef: Einfluss des Aderlasses und der Transfusion auf den Wert des Atmungsstoffwechsel, Jahresb. ü. d. Fortschr. d. Thierchem. (Maly's), 1906, p. 561.

6. Fredericq: De l'action physiologique des soustractions sanguines, Jahresb. ü. d. Fortschr. d. Thierchem. (Maly's), 1887, p. 377.

7. Hari: Der Einfluss grosser Blutverluste auf die Kohlensäure—und Wasserauscheidung und Wärmeproduction, Arch. f. d. ges. Physiol. (Pflüger's), 1909, pp. 130, 187.

8. Magnus-Levy: Ueber den Stoffwechsel bei einem leukämischen Mannes, Ztschr. f. Biol., 1869, v, 319.

9. Kraus: Ueber den Einfluss von Krankheiten auf den respiratorischen Gaswechsel, Ztschr. f. klin. Med., 1893, xxii, 458.

10. Bohland: Ueber den respiratorischen Gaswechsel bei verschiedenen Formen der Anämie, Berl. klin. Wchnschr., 1893, xviii, 417.

11. Thiele and Nehring: Gaswechsel bei anämischen zuständen, Ztschr. f. klin. Med., 1896, xxx, 41.

12. Magnus-Levy: Der Einfluss von Krankheiten auf den Energiesaushalt im Ruhestand, Ztschr. f. klin. Med., 1906, lx, 179.

13. Grafe: Die Steigerung des Stoffwechsels bei chronischer Leukämie, Arch. f. klin. Med., 1911, cii, 406.

an amazing augmentation in leukemia. The results of these observers will receive further consideration.

EXPERIMENTAL PROCEDURE

The six cases of anemia which we wish to present were all studied from sixteen to eighteen hours after the last meal. The patients were at rest and in the lying posture. They were allowed to turn in bed occasionally and move their arms a little. While it is desirable that there should be no unnecessary movements, we believe the subject should be as comfortable as the conditions of the experiment will permit.

The exact routine previous to the actual observation has received detailed consideration in another place.[14] The body temperature was measured by means of an electric resistance thermometer placed in the rectum. Surface thermometers were not used. It has been found that when there are no rapid fluctuations in body temperature the rectal temperature is the more reliable but is by no means absolutely satisfactory. Owing to the limitations of the rectal thermometer, and its failure to register accurately the mean temperature changes of the body, we still use the method of indirect calorimetry as a standard, for reasons previously discussed.

HISTORIES OF PATIENTS

Case 1.—*History.*—Daniel V. (splenic anemia, congenital syphilis), aged 21 years, elevator boy, white, French West Indies, admitted April 16, 1913, discharged July 30, 1913, had severe dysentery in 1897, and tropical fever with black stools in 1902. He had pain in the left side in 1910. He came to New York in 1912. A fine rash appeared on the body, March 30, 1913, and the patient became pale. March 27 and again two weeks later, he vomited blood.

Physical Examination.—April 16, the patient was tall and thin, with porcelain colored skin. Soft systolic murmur. Spleen palpable 7 cm. below costal margin. Hemoglobin, 25 per cent.; erythrocytes, 1,700,000. Differential count normal except for 1.5 per cent. myelocytes. Wassermann reaction positive. April 19, transfusion, 500 c.c. Spleen larger. April 23, transfusion, 750 c.c. April 24, spleen 11 cm. below costal margin in midclavicular line. Dark stools. April 26, transfusion, 760 c.c. Hemoglobin, 25 per cent.; erythrocytes, 1,976,000. May 9, patient put in the calorimeter. Blood pressure: systolic, 108; diastolic, 48; temperature 99-100; pulse 96; respiration 20; stools, four or five every day. Wassermann positive.

The spleen was removed several weeks later, and the patient improved rapidly. He was seen a year later in good health.

Case 2.—*History.*—Andrew K.[15] (pernicious anemia), aged 27, plumber, entered the hospital Sept. 10, 1911, with a high grade of anemia. He improved

14. Gephart, F. C., and Du Bois, E. F.: Clinical Calorimetry, Fourth Paper, The Determination of the Basal Metabolism of Normal Men and the Effect of Food, The Archives Int. Med., 1915, xv, 835.

15. Case reported by Coleman and Hartwell: Med. Rec., New York, 1914. lxxxv, 1160.

under the syrup of ferrous iodid, sodium cacodylate and Blaud's pills. He was discharged Nov. 1, 1911, and readmitted June 23, 1913. He worked as street car conductor but had to stop work because of weakness. There was no history of syphilis.

Physical Examination.—The patient's skin was lemon yellow, there was extensive pigmentation, and the teeth were in bad condition. The spleen was three fingers' breadth below the costal margin. Jan. 24, 1913, the hemoglobin was 50 per cent.; erythrocytes, 1,600,000; marked anisocytosis and poikilocytosis. Slight polychromatophylia. Leukocytes, 6,000. Stools negative. During the ensuing four months there were low, continued fever, attacks of diarrhea, progressive weakness and high pulse rate. Several transfusions were made. The last transfusion was interrupted by hemolysis. Two hours later severe chills and temperature of 103.8. Four hours later, 2 ounces of bloody urine.

Treatment and Course.—July 8, normoblasts 26 to every 100 leukocytes. Leukocytes, 2,000; polymorphonuclears, 64 per cent.; lymphocytes, 30 per cent.; large mononuclears, 3 per cent. October 29, splenectomy. Cytologic details essentially those of erythrogenesis and myelogenesis. November 3, lemon yellow color disappeared. Picture of severe secondary anemia. November 17, leukocytes 12,000. December 6, leukocytes 16,000. December 29, hemoglobin, 27 per cent.; erythocytes, 1,280,000; normoblasts, 51, and megaloblasts 11 to every 200 leukocytes. Jan. 6, 1914, leukocytes, 22,400; January 13-29, neosalvarsan. Patient grew weaker. February 25, hemoglobin, 18 per cent.; erythrocytes, 1,264,000. Normoblasts 111 and megaloblasts 16 to every 200 leukocytes. March 11 and 17, patient put in calorimeter. Pulse during March ranged from 100 to 124; respirations from 24 to 28; blood pressures: systolic, 142; diastolic, 50 (March 27); temperature, from 99 to 100. April 24, patient looked and felt better. Beginning to sit up. April 28, Wassermann reaction positive. Patient died December, 1915.

CASE 3.—*History.*—Martin C. (pernicious anemia, transverse myelitis), driver, aged 32, admitted Jan. 8, 1915, died December, 1915, complained chiefly of weakness, shortness of breath, palpitation and paralysis of legs. In 1905 he slipped and had a bad fall which left him with a persistent pain between the shoulders. One year later the pains suddenly disappeared, but his legs began to grow numb and he lost good control of his feet. Soon after he was unable to walk and unable to control his bowels. In 1912 he began to grow stronger, and was able to walk with crutches. In February, 1914, he noticed general weakness. In December, a month before admission, he began to suffer from anemia, dyspnea, palpitation, nausea and insomnia.

Physical Examination.—January 8, the patient was very pale, poorly developed and poorly nourished. Cardiac impulse forceful and diffuse. Apex in fifth space 5.6 cm.; left border 12 cm. from midsternal line; base in third space. Presystolic thrill over precordium. Presystolic murmur and systolic murmur at apex, the latter transmitted to axilla. Systolic murmur at aortic area. Corrigan pulse. Spleen palpable. Legs paralyzed, wasted and atrophic. Babinski reflex present. Lymph nodes generally enlarged. Incontinent of urine. January 13, eyegrounds showed presence of old retinal hemorrhages. January 20, erythrocytes, 650,000; normoblasts, 47; megaloblasts, 6. Anisocytosis, poikilocytosis and polychromatophylia marked. January 29, patient in the calorimeter. January 28 to February 23, temperature from 99 to 101; pulse from 100 to 124; respirations, from 20 to 30. February 2, hemoglobin 23.4 per cent. February 10, fluid on left side of chest. Thoracentesis. February 16, hemoglobin, 20 per cent. February 27, dulness on left side persisted. March 17, heart not enlarged. Systolic murmur over second left space and over apex. Edge of liver felt indistinctly at umbilicus. March 23, erythrocytes, 472,000; leukocytes, 2,600; anisocytosis and poikilocytosis very marked. May 4, patient put in calorimeter. Hemoglobin, 21 per cent. Apex impulse diffuse. Left limit dul-

ness, fifth space, 13 cm.; fourth space, 11.8 cm.; third space, 10 cm.; right limit, 2.8 cm. from midsternal line. Loud booming systolic murmur at apex. To left of sternum there was a soft blowing sound in diastole. Posteriorly left side flatness below angle of scapula. Patient later got up in a chair and dressed himself. Slightly jaundiced. April 24 to May 22, temperature normal to 100; pulse 72 to 115; respiration, 20 to 24. At necropsy in December, 1915, a bony tumor was found pressing on the spinal cord, causing a transverse myelitis.

CASE 4.—*History.*—Bartolo D. (pernicious anemia), aged 50, laborer, admitted Feb. 22, 1915, discharged March 21, 1915, complained chiefly of weakness, and pain in abdomen. Four months ago he felt sick but was able to continue work.

Physical Examination.—February 22, poorly nourished. Appearance chronically ill. Skin of peculiar greenish yellow. Conjunctiva pale. Heart regular in rate, force and rhythm. Soft systolic murmur over entire precordium. Pulse regular in rate, force and rhythm. Tension low. Vessel walls thickened. Slight distention of abdomen. Extremities wasted. General lymphatic enlargement. February 23, blood pressure 95 (systolic). February 24, temperature rose to 100.7, after which it remained below 100. Pulse varied from 80 to 100. February 28, blood pressure, systolic, 92; diastolic, 70. March 4, stools negative. March 5, red cells 1,328,000; hemoglobin, 27 per cent.; megaloblasts, 6; leukocytes, 4,200; polymorphonuclears, 71; lymphocytes, 28. March 15, condition unchanged. Patient put in calorimeter. Complained of weakness and toothache. Stools large, possibly due to poor absorption. On strong positive nitrogen balance. March 18, red cells, 2,200,000; hemoglobin, 44 per cent. Wassermann reaction negative.

CASE 5.—*History.*—Daniel O. (pernicious anemia, mitral stenosis and insufficiency), aged 38, steam fitter, admitted April 11, 1915, discharged May 10, 1915, complained chiefly of dizziness and weakness. Pain in lower lumbar region. The patient was moderately alcoholic. In 1905, kidney trouble. Had been able to work hard during past year. For several months had had a dry cough; slight impairment of vision. In March friends noticed pallor. April 4, 1915, pains in lower lumbar region with fainting and dizziness.

Physical Examination.—April 11th, patient was pale and sallow. Looked sick. Conjunctiva edematous. Face puffy. Teeth bad. Lungs showed signs of chronic bronchitis and passive congestion, especially posteriorly. Sibilant and sonorous râles. Heart sounds of poor muscular quality. Presystolic thrill and systolic murmur over apex, the latter transmitted to the back. Aortic second somewhat accentuated. Pulse regular in rate and rhythm, and of fair force. Liver two finger' breadths below umbilicus. Spleen not felt, but area of dulness increased. April 15, red cells, 1,800,000; hemoglobin, 40 per cent.; polymorphonuclears, 56; transitionals, 16; lymphocytes, 16; large mononuclears, 8; eosinophils, 2.5; mast cells, 1.5; megaloblasts, 2. Respirations, 20. April 26, patient put in calorimeter. Felt better than on admission. Not strong enough to work. Lemon tinted color. Eyelids puffy. Could walk up one flight of steps without stopping. May 4, blood pressure: systolic, 130; diastolic, 80. May 10, no complaints. Discharged. (Urine showed faint trace albumin; occasional casts, and numerous leukocytes.)

DISCUSSIONS OF RESULTS

The average figures for the normal metabolism have been given in the thirteenth paper of this series.

In pernicious anemia we have obtained an increase of metabolism in all of the five cases. The figures vary from 2 to 33 per cent. above the average normal. The highest heat production was found in

Martin C. (Case 3). Unfortunately his temperature was a trifle above the normal, and he was also a little restless during this observation, as is indicated by the work-adder, the readings of which were 25, 22 and 31 for the first, second and third hours, respectively. A reading of 7 cm. is equivalent to turning from back to side. A correction of at

TABLE 1.—DETAILS OF—

Subject, Date, Weight, Surface Area, Linear Formula	Period	End of Period	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.
Case 1 (Daniel V.) 5/9/13 61.35 Kg.	Prelim.	9:40	.....	.....	.....	.....	.....	......	.....
	1	10:40	23.22	20.55	0.822	30.86	0.323	68.82	59.74
	2	11:40	24.06	22.18	0.789	31.86	0.323	73.71	63.92
	3	12:40	24.05	21.89	0.799	32.40	0.323	72.92	65.51
Case 2 (And. K.)... 8/11/14 52.72 Kg.	Prelim.	10:55	.....	.....	.....	.....	.....	......	.....
	1	11:55	25.84	22.53	0.834	22.16	0.519	75.38	63.18
	2	12:55	25.45	21.91	0.845	25.33	0.519	73.47	72.61
Andrew K. .... 8/27/14 52.03 Kg.	Prelim.	10:45	.....	.....	.....	.....	.....	......	.....
	1	11:45	23.55	20.60	0.831	28.54	0.307	69.21	73.40
	2	12:45	24.60	21.30	0.840	28.55	0.307	71.75	72.89
Case 3 (Martin C.) 1/29/15 47.80 Kg. 1.49 Sq. M.	Prelim.	.....	.....	.....	.....	.....	.....	......	.....
	1	12:02	26.13	23.62	0.805	22.67	0.364	78.68	69.35
	2	1:02	24.04	22.66	0.772	27.44	0.560	74.49	76.01
	3	2:02	26.57	24.64	0.784	31.76	0.560	81.43	79.65
Martin C. .... 5/4/15 44.21 Kg 1.44 Sq. M.	Prelim.	.....	.....	.....	.....	.....	.....	......	.....
	1	12:16	22.02	19.12	0.838	27.39	0.237	64.41	60.69
	2	1:16	20.66	16.87	0.891	25.61	0.237	57.53	55.93
Case 4 (Bart. D.).. 3/15/15 41.80 Kg. 1.39 Sq. M.	Prelim.	.....	.....	.....	.....	.....	.....	......	.....
	1	12:18	16.28	13.76	0.861	16.01	0.224	46.55	52.47
	2	1:18	16.68	15.27	0.796	17.06	0.224	50.79	58.64
	3	2:18	17.65	15.41	0.833	16.65	0.224	51.84	51.23
Case 5 (Daniel O.) 4/26/15 60.05 Kg. 1.66 Sq. M.	Prelim.								
	1	12:30	21.64	20.57	0.765	31.33	0.398	67.80	40.68
	2	1:30	22.80	21.55	0.769	31.30	0.398	71.06	46.39

least 10 per cent. is therefore necessary to account for these two factors.

Only in Cases 2 and 3 (Andrew K., and Martin C.) did the heat production exceed the range of normal variation. Both are examples of severe anemia from the clinical point of view, with a hemoglobin

percentage of less than 25. It is of interest to note that Martin C. had practically lost the use of his legs, and that his extremities were wasted and atrophic as the result of a transverse myelitis.

Bartolo D. and Daniel O. (Cases 4 and 5) cannot be said to show a pathologic increase of metabolism. It is not likely that the insufficiency of the mitral valve in Daniel O.'s case could in any way have affected his metabolism. Clinically the condition of these two patients was not so severe. Their hemoglobin approximated from 40 to 44 per cent. of the normal. Daniel O. was able to walk up one flight of steps without stopping on the day of the observation.

—CALORIMETER EXPERIMENTS

Direct Calorimetry (Rectal Temp.), Cal.	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks Surface Area Meeh's Formula
					Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M.	
.....	37.10	...	....	.....	..	..	..	.....	.....	Basal; Sq. M. = 1.915
65.42	37.22	...	....	0.824	12	53	35	1.12	35.94	Very quiet; slept most of time
67.73	37.30	...	....	0.787	12	64	24	1.20	38.49	Slightly restless
70.15	37.40	...	....	0.798	12	60	28	1.19	38.08	Restless
.....	37.13	...	....	.....	..	..	..	.....	.....	Basal; Sq. M. = 1.781
67.13	37.23	102	14.7	0.842	18	44	38	1.43	43.55	
77.47	37.35	108	48.8	0.855	19	40	41	1.38	42.44	
.....	37.30	...	....	.....	..	..	..	.....	.....	Basal; Sq. M. = 1.706
66.57	37.15	101	34.6	0.835	12	49	39	1.38	40.57	Asleep most of 1st period
72.55	37.15	98	41.0	0.845	11	47	42	1.38	42.06	Asleep half of 2d period; restless in sleep
.....	37.90	...	....	.....	..	..	..	.....	.....	Basal; Sq. M. = 1.622
76.59	38.06	107	24.5	0.800	12.3	59.7	28.0	1.015	48.51	Somewhat restless
75.59	38.05	104	22.0	0.760	19.9	65.3	14.8	0.961	45.96	Restless 5 min.
77.43	38.01	105	31.7	0.740	18.4	72.1	9.05	1.041	49.77	Restless 5 min.
.....	.....	...	....	.....	..	..	..	.....	.....	Basal; Sq. M. = 1.539 (M)
59.35	36.60	91	24.0	0.841	9.4	49.1	41.2	1.801	.....	Fairly quiet; voided
55.73	36.60	88	6.0	0.902	10.7	30.8	58.8	1.457	.....	Very quiet
.....	37.24	...	....	.....	..	..	..	.....	.....	Basal; Sq. M. = 1.483
52.24	37.24	71	7.0	0.869	12.7	38.6	48.7	1.114	31.39	Very quiet
50.94	37.23	67	12.0	0.793	11.7	53.1	25.2	1.215	34.25	Quiet
58.03	37.20	69	6.0	0.837	11.4	48.2	40.4	1.240	34.96	Quiet
.....	.....	...	....	.....	..	..	..	.....	.....	Basal
61.08	37.04	78	15.0	0.757	15.6	68.9	15.5	1.129	35.91	Quiet
62.64	37.00	76	16.0	0.763	14.8	69.5	15.7	1.183	37.64	Quiet

TABLE 2.—SUMMARY OF CALORIMETER EXPERIMENTS; AVERAGES OF PERIODS; ALL BASAL EXPERIMENTS ON MEN

Subject and Date	Weight, Kg.	Age, Yrs.	Aver. Calories per Hour, Indirect	Average R. Q.	Indirect Calorimetry Average per Hour: Average Calories per Kg.	Per Sq. M. Meeh's Formula	Per Cent. Divergence from Average Normal Basal Meeh	Average Normal Basal Meeh	Per Sq. M. Linear Formula	Per Cent. Divergence for Average Normal Basal Lin.	Average Normal Basal Lin.	Total Calories each Experiment: Indirect	Direct	Per Cent. of Divergence of Direct from Indirect	Remarks
Case 1 (Daniel V.) 5/9/13	61.35	21	71.81	0.803	1.17	37.50	+ 8	34.7	.....	......	39.7	215.45	203.30	—5.5	Slightly restless
Case 2 (Andrew K.) 3/11/14	52.72	27	74.42	0.839	1.41	42.99	+24	34.7	.....	......	39.7	148.85	144.65	—2.8	Fairly quiet
3/27/14	52.03	27	70.48	0.835	1.36	41.31	+19	34.7	.....	......	39.7	140.96	139.12	—1.3	Asleep
Case 3 (Martin O.) 1/29/15	47.80	32	78.20	0.787	1.636	48.21	+40.1	34.7	52.59	+32.5	39.7	234.60	229.61	2.1	Slightly restless
5/ 4/15	44.21	32	60.97	0.865	1.379	39.62	+14.2	34.7	42.43	+ 6.9	39.7	121.94	115.08	5.3	Quiet
Case 4 (Bartolo D.) 3/15/15	41.80	50	49.73	0.830	1.189	33.53	+ 8.8	30.8	35.91	+ 2.0	35.2	149.18	156.21	+4.8	Quiet
Case 5 (Daniel O.) 4/26/15	60.05	38	69.48	0.767	1.156	36.78	+ 6.0	34.7	41.90	+ 5.5	39.7	138.86	123.72	—10.9	Quiet
												1,149.84	1,111.69	—3.3	

Daniel V. (Case 1) is a case of splenic anemia with congenital syphilis. At present we do not know what bearing the history of syphilis has in this connection.

The literature affords considerable evidence that the methods of direct and indirect calorimetry may show remarkable agreement. This agreement has been shown by Rubner and Lusk on dogs; by Atwater and Benedict on man; by Carpenter and Murlin on parturient women, and by Howland on babies. Gephart and Du Bois,[14] in their study of normal men, found that the totals of indirect and direct heat production came within 0.17 per cent. of each other, and that even in one hour periods the agreement was striking.

It is of the utmost importance to determine whether the same agreement can be demonstrated in disease. Coleman and Du Bois,[16] in their series of sixty experiments on typhoid patients, obtained an average divergence in individual experiments of 5 per cent., and a total divergence of 2.2 per cent.

In our series of anemic patients (Table 2) the total divergence between direct and indirect calorimetry is about 3.3 per cent. In three of the observations the variation is from 1 to 3 per cent. The greatest discrepancy is 12 per cent. In hourly periods the least divergence is 1 per cent., the greatest 12 per cent. In the total there were seventeen one hour periods. In ten of these periods the two methods agreed within 2.5 per cent.; in two, within 8 per cent.; in four, within from 10 to 12 per cent.

The relationship between the volume of carbon dioxid produced and the volume of oxygen consumed justifies the inference that there is no profound qualitative change in the metabolism of pernicious anemia. There is no evidence of increased protein consumption. The nonprotein respiratory quotients vary from 0.76 to 0.87, indicating that fat and carbohydrate are burned to the same end-products as in health.

In Table 3 we have tabulated the results obtained by others in a variety of anemias. In all cases in which the heat production was not given, we have converted the oxygen consumption per kilogram per minute into calories per square meter per hour, on the assumption that 15 per cent. of the calories are derived from protein. The area of body surface was computed according to Meeh's formula. We have indiscriminately applied the normal figure 34.7 calories per square meter per hour to all observations in arriving at the percentage increase or decrease in metabolism except in our own cases, in which the linear formula standards have been used in all cases measured by this method. The standard normal of 34.7 is not strictly accurate,

16. Coleman, Warren, and Du Bois, E. F.: Clinical Calorimetry, Seventh Paper, Calorimetric Observations on the Metabolism of Typhoid Patients With and Without Food, The Archives Int. Med., 1915, xv, 887.

TABLE 3.—SUMMARY OF RESULTS OF VARIOUS INVESTIGATORS

Observer	Disease	Patient	Sex*	Age, Years	Weight, Kg.	Temperature	Pulse	Resp.	Hb, per Cent.	R. Q.	Calories per Sq. M. per Hour Meeh's Formula	Per Cent. Above or Below Normal	Remarks
Grafe, E.	Lymph. Leuk.	T. S. 1a	♂	50	66.0	36.2	100	36	..	0.700	68.66	+98	Very dyspneic; restless at times
Grafe, E.	Lymph. Leuk.	T. S. 1b	♂	50	67.8	36.4	100	32	..	0.840	52.00	+50	
Grafe, E.	Lymph. Leuk.	T. S. 1c	♂	50	68.5	36.5	90	34	..	0.831	48.66	+40	
Grafe, E.	Lymph. Leuk.	G. K. 2	♂	56	75.0	36.2	80	22	..	0.881	36.75	+ 6	
Grafe, E.	Lymph. Leuk.	G. L. 3a	♀	65	48.2	36.0	80	20	..	0.898	44.45	+28	Asleep most of time
Grafe, E.	Lymph. Leuk.	G. L. 3b	♀	65	48.0	36.2	88	24	..	0.820	46.92	+35	Asleep most of time
Grafe, E.	Lymph. Leuk.	M. T. 4	♂	49	63.8	37.2	82	22	..	0.851	65.04	+87	Restless now and then
Grafe, E.	Lymph. Leuk.	M. D. 5	♂	56	65.8	36.6	88	—	..	0.807	49.83	+44	
Magnus-Levy.......	Lymph. Leuk.	J.	♂	49	53.5	....	..	..	..	0.783	45.18	+30	Av. 8 observations
Grafe, E.	Myel. Leuk.	F. N. 6	♀	32	64.3	36.6	82	20	..	0.783	58.20	+53	
Grafe, E.	Myel. Leuk.	M. H. 7	♀	38	51.0	36.7	86	18	..	0.777	49.79	+43	
Grafe, E.	Myel. Leuk.	H. B. 8	♂	48	57.5	36.5	80	15	..	0.814	42.33	+22	
Kraus, F.	Spl. Med. Leuk. ...	M. B.	♂	60	55.0	Normal	86	12	50	0.790	48.67	+40	
Kraus, F.	Spl. Med. Leuk. ...	M. B.	♂	60	55.0	Normal	86	12	50	0.772	46.40	+33	
Kraus, F.	Spl. Med. Leuk. ...	M. B	♂	60	55.0	Normal	86	12	50	0.777	45.83	+32	
Kraus, F.	Spl. Med. Leuk. ..	W. K.	♂	37	74.7	Normal	100-108	14	45	0.811	47.80	+38	
Kraus, F.	Spl. Med. Leuk. ...	W. K	♂	37	74.7	Normal	100-108	14	45	0.814	46.72	+35	
Kraus, F.	Spl. Med. Leuk. ...	W K.	♂	37	74.7	Normal	100-108	15	45	0.805	49.37	+42	
Kraus, F.	Splenic Leuk.	S. W.	♀	34	61.0	Normal	80	14	45-50	0.866	49.74	+43	
Kraus, F.	Splenic Leuk.	S. W.	♀	34	61.0	Normal	80	12	45-50	0.808	49.17	+42	
Bohland............	Splenic Leuk.	H.	♀	38	53.5	Normal	114-120	22-24	—	0.800	51.84	+49	6:30 N
Bohland............	Splenic Leuk.	H.	♀	38	53.5	Normal	114	22-26	—	0.890	57.80	+66	6:15 N
Bohland............	Splenic Leuk.	H.	♀	38	53.5	Normal	108	20-23	—	0.840	56.71	+63	6:45 N
Bohland............	Splenic Leuk.	H.	♀	38	53.5	Normal	112-116	19-23	—	0.810	54.80	+58	10:00 N
Kraus, F.	Chlorosis..........	V. H.	♀	20	49.0	Normal	78-84	16	45	0.710	41.17	+19	
Kraus, F.	Chlorosis..........	V. H	♀	20	49.0	Normal	78-84	18	45	0.735	44.29	+28	
Magnus-Levy.......	Chlorosis..........	1. G	♀	20	44.8	....	..	..	..	0.806	34.01	— 0.2	18 observations

Magnus-Levy........	Chlorosis..........	M. W.	♀	18	53.5	....	..	..	..	0.794	36.68	+ 7	8 observations
Thiele and Nehring..	Chlorosis..........	B.	♀	22	57.5	Normal	80	12	85	0.902	31.76	− 8	Chr. otitis media
Thiele and Nehring..	Chlorosis..........	B.	♀	22	57.5	Normal	80	12	85	0.805	31.21	−10	Chr. otitis media
Thiele and Nehring..	Chlorosis..........	B.	♀	22	57.5	Normal	80	13	85	0.858	31.97	− 8	Chr. otitis media
Thiele and Nehring..	Chlorosis..........	P.	♀	18	58.5	Normal	90-100	18	55	0.925	27.98	−19	
Thiele and Nehring..	Chlorosis..........	P.	♀	18	58.5	Normal	90-100	18	55	0.900	27.89	−19	
Thiele and Nehring..	Chlorosis..........	P.	♀	18	58.5	Normal	90-100	24	55	0.804	28.61	−17	Complained of toothache
Thiele and Nehring..	Chlorosis..........	P.	♀	18	58.5	Normal	90-100	24	55	0.779	29.68	−15	Complained of toothache
Thiele and Nehring..	Chlorosis..........	P.	♀	18	59.0	Normal	90-100	20	55	0.825	28.84	−17	
Thiele and Nehring..	Chlorosis..........	P.	♀	18	59.0	Normal	90-100	20	55	0.806	29.08	−16	
Kraus, F.	Sec. anemia........	L. S.	♂	33	61.0	Normal	88-100	18	25	0.752	40.78	+17	
Kraus, F.	Sec. anemia........	L. S.	♂	33	61.0	Normal	88-100	14	25	0.763	39.48	+14	
Kraus, F.	Sec. anemia........	L. S.	♂	33	61.0	Normal	88-100	14	25	0.746	43.99	+27	
Magnus-Levy........	Sec. anemia........	G. S.	♀	30	44.1	....	..	..	..	0.860	33.77	− 3	2 observations
Magnus-Levy........	Sec. anemia........	W. R.	♂	40	63.4	....	..	..	..	0.779	37.27	+ 7	4 observations
Magnus-Levy........	Sec. anemia........	B. L.	♀	27	47.7	....	..	..	..	0.775	30.58	−12	8 observations
Thiele and Nehring..	Sec. anemia........	B.	♀	—	47.5	Normal	—	19	—	0.877	35.59	+ 3	Very anemic after hemorrhoid bleeding; slept part of time
Thiele and Nehring..	Sec. anemia........	B.	♀	—	47.5	Normal	—	18	—	0.850	34.53	− 0.5	
Thiele and Nehring..	Sec. anemia........	B.	♀	—	47.5	Normal	—	17	—	0.864	36.41	+ 5	Slept part of time
Kraus, F.	Pernicious anemia	A. D.	♀	46	54.0	Normal	96-108	14	30	0.710	37.52	+ 8	
Kraus, F.	Pernicious anemia	A. D.	♀	46	54.0	Normal	96-108	15	30	0.709	40.55	+17	
Magnus-Levy........	Pernicious anemia	M.	♀	40	44.7	....	..	..	..	0.813	38.87	+12	6 observations
Magnus-Levy........	Pernicious anemia	W.	♀	45	42.5	....	..	..	..	0.738	36.17	+ 4	1 observation
Authors.............	Pernicious anemia, splenic	1 (D. V.)	♂	21	61.35	37.25	96	20	25	0.808	37.50	+ 8	
Authors.............	Pernicious anemia	2 (A. K.)	♂	27	52.72	37.25	100-124	24-28	20	0.839	42.99	+24	
Authors.............	Pernicious anemia	2 (A. K.)	♂	27	52.03	37.20	100-124	24-28	20	0.835	41.31	+19	
Authors.............	Pernicious anemia	3 (M. C.)	♂	32	47.80	38.00	100-124	20-30	23	0.787	48.07	+33	
Authors.............	Pernicious anemia	3 (M. C.)	♂	32	44.21	36.60	72-115	20-24	21	0.865	39.61	+ 7	
Authors.............	Pernicious anemia	4 (B. D.)	♂	50	41.80	37.30	80-100	18-24	44	0.830	33.53	+ 2	
Authors.............	Pernicious anemia	5 (D. O.)	♂	38	60.05	37.02	..	..	40	0.767	36.78	+ 6	

* In this column ♂ denotes male; ♀, female.

inasmuch as many of the subjects were women. In sixty-eight women, Benedict, Emmes, Roth and Smith found the heat production to be 32.2 calories per square meter per hour, or 7 per cent. lower than in men.

It will be observed that Magnus-Levy[12] and Kraus[9] found the metabolism in pernicious anemia from 4 to 17 per cent. above the normal. The correction for sex would increase the percentage in the case of Magnus-Levy, but would leave it unaffected in the case of Kraus, because his subjects sat on a chair, a posture which sometimes raises the metabolism.

It is interesting to notice the striking contrast between the metabolism of pernicious anemia and that of leukemia. Both Bohland[10] and Kraus[9] were led to erroneous conclusions regarding the metabolism of leukemia. This is to be explained by the fact that Bohland allowed a variation of over 30 per cent. from the average consumption of oxygen of a normal individual at rest. Kraus' upper physiologic limit of 5.75 c.c. oxygen per minute is rather high. If we interpret their results with reference to the modern base line in terms of heat units, their leukemic patients show a marked rise of metabolism. Bohland, who used the Zuntz-Geppert apparatus, states that all of his experiments were performed from five to six hours after the midday meal, or from three to four hours after breakfast, or else in the morning in a "nüchtern" state. Three of the observations which we have tabulated came between 6 and 7 in the evening and one at 10 o'clock in the morning, so that in all four the metabolism was still affected by the previous ingestion of food. Kraus, who also employed the Zuntz-Geppert method, allowed his patients to sit upright on a chair. This in itself would doubtless elevate the metabolism somewhat.

Grafe[13] used a modified form of the Jaquet apparatus in his experiments on leukemic patients. Eliminating those experiments, in which the subject was dyspneic and very restless, we obtain figures from 6 to 50 per cent. above the normal of 34.7.

Kraus,[9] Magnus-Levy[12] and Thiele and Nehring[11] have investigated chlorosis and secondary anemia. When we express the oxygen absorption which Kraus found in chlorosis, and secondary anemia in terms of calories, the metabolism is abnormally high. We must again remember that Kraus permitted his patients to sit during the observation. Magnus-Levy's results do not exceed the normal bounds. In the work of Thiele and Nehring we meet for the first time a lowered metabolism in an anemic state, although they, themselves, believed that a diminution in the oxygen intake could not be demonstrated in chlorosis.

COMPENSATORY FACTORS IN ANEMIA

It is clear from the foregoing experimental results that a reduction in the hemoglobin does not preclude the possibility of either a normal or an augmented metabolism. There is no evidence that metabolism runs its course on a lower plane in anemia. The demand for oxygen may far exceed the demand in health. How, then, is the requirement met?

In health, oxygen combines with hemoglobin by reason of chemical affinity. It is conceivable that in disease Nature may resort to physical means of increasing the combining capacity of hemoglobin. Such a conception, however, appears improbable from a comparison of Butterfield's[17] work with that of Peters.[18] Butterfield found that the ratio of CO (or O_2): Fe averaged 399 in eleven patients, some of whom were anemic. This agrees remarkably well with the average specific oxygen capacity of 411, which Peters obtained with normal blood, using quite a different method. We may conclude that in anemia, physical means play no rôle in the absorption of oxygen apart from the slight amount taken up by the plasma in physical solution.

Normally the supply of oxygen to the tissues is beyond the immediate requirement. In anemia when the hemoglobin content is low and the volume per cent. of oxygen is correspondingly diminished, the consumption of oxygen remains normal, or may even be above the normal. Since no means of augmenting the oxygen carrying capacity per unit of blood has been demonstrated, it is manifest that the margin of safety must be encroached upon and that the blood must return to the heart in various degrees of asphyxia. That this is actually the case appears in the work of Mohr,[18] Morawitz and Röhmer[20] and Kraus and Chovstek.[21] In certain forms of anemia, under conditions of rest and with a metabolism near normal, the extra quota of oxygen which Nature has generously provided would suffice. A simple calculation, however, will show that in some patients other factors must be brought into play. Let us take, for instance, the case of Andrew K. (Case 2), whose metabolism was high and whose hemoglobin was 20 per cent. of the normal. With this amount of hemoglobin, 100 c.c.

17. Butterfield: Ueber die Lichtextinktion, das Gasbindungsvermögen und den Eisengehalt des menschlichen. Blutfarbstoffes in normalen und krankhaften Zuständen, Ztschr. f. physiol. Chem., 1909, lxii, 173.

18: Peters: Chemical Nature of Specific Oxygen Capacity in Hemoglobin, Jour. Physiol., 1912, xliv, 131.

19. Mohr: Ueber regulierende und compensirende Vorgänge im Stoffwechsel der Anämischen, Ztschr. f. exper. Path. u. Therap., 1906, ii, 435.

20. Morawitz and Röhmer: Ueber die Sauerstoffversorgung bei Anämien, Deutsch. Arch. f. klin. Med., 1908, xciv, 529.

21. Kraus and Chovstek: Ueber den Einfluss von Krankheiten auf den respiratorischen Gaswechsel, Ztschr. f. klin. Med., 1893, xxii, 573.

of blood would contain 3.7 c.c. of oxygen. Assuming a pulse rate of 70 and an average normal output per beat of 50 c.c., the minute output of oxygen would be 130 c.c. His actual need was about twice this, namely, 252 c.c. oxygen per minute as determined by the calorimeter. His pulse rate averaged 101, and therefore his output per beat must have been at least 66 c.c. to supply enough oxygen to meet the demands calculated according to the formula: Pulse Rate $\times$ Output per beat per cent. $O_2 = 252$.

Plesch[22] and Mohr[19] call attention to the increased output and pulse frequency in anemia. A more liberal supply of blood to the tissues may at times be favored by a greater respiratory volume. That the depth of respirations increase has been noticed by Jurgensen,[23] Kraus[9] and others. It is chiefly of value in facilitating the filling of the right heart. Its effect on the absorption of oxygen is negligible.

THE CAUSE OF HIGH METABOLISM IN ANEMIA

In anemia we frequently encounter signs of rapid regeneration. Normoblasts and megaloblasts may be present in secondary anemia, but are especially characteristic of pernicious anemia. Whether or not this is a reversion to the embryonic type of cell formation, the fact remains that these cells constitute a considerable mass of young tissue in the process of development. Their number in the peripheral blood is no measure of those present in the body. In the blood of rabbits with subchronic anemia experimentally induced there is a pronounced consumption of oxygen and production of carbon dioxid in vitro. This Morawitz[24] attributes to the presence of nucleated red cells.

In the leukemias we also see nucleated red cells, but their number is insignificant compared with the enormous increase in the white cells. Grafe[18] believes that the white blood cells are an important factor in the extra heat production of leukemia.

Zuntz, Löwy, Müller and Caspari[25] show that muscles poorly supplied with oxygen are functionally less efficient. Accessory muscles are called on to cooperate in the accomplishment of any task. The mechanism of the vital function of respiration and circulation becomes more complex. Proper breathing requires the activity of muscles that

22. Plesch: Haemodynaemische Studien, Ztschr. f. exper. Path. u. Therap., 1909, vi, 526.
23. Jürgensen: In von Noorden's Pathologie der Stoffwechsel, Ed. 1, 1893, p. 335.
24. Morawitz: Ueber Oxydationsprozesse im Blut, Arch. f. exper. Path. u. Pharmakol, 1909, lx, 298.
25. Zuntz, Löwy, Müller and Caspari: Hohenklima und Bergwanderungen, Berlin, 1906, Table XII, p. 435.

ordinarily play no rôle in respiration. Again, the respiratory muscles may serve in securing a more efficient circulation. In general, activity implies unusual effort, and hence the demand for additional oxygen.

CONCLUSIONS

Three mild cases of pernicious anemia showed very slight increase in the metabolism. In two severe cases the demand for oxygen was from 7 to 33 per cent. above the normal average.

The basal metabolism of pernicious anemia is lower than that of leukemia, but, as a rule, higher than that of secondary anemia.

The agreement between the direct and indirect calorimetry as well as the respiratory quotients indicates that the basal metabolism of pernicious anemia is qualitatively identical with the normal.

Although the demand for oxygen may be increased, the compensatory processes in uncomplicated cases of pernicious anemia are capable of meeting the demand in spite of a greatly diminished hemoglobin content.

There is some ground for the belief that the height of metabolism is a measure of the severity of the clinical pictures.

477 First Avenue.

CLINICAL CALORIMETRY

SIXTEENTH PAPER

THE BASAL METABOLISM OF PATIENTS WITH CARDIAC AND RENAL DISEASE *

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The literature contains extremely few reports of observations on the metabolism of patients with heart disease. The work most frequently referred to is a monograph of Kraus.[1] This study of the effect of fatigue in various pathologic conditions contains observations on the gaseous metabolism of three cardiac patients while at rest and while working on an ergograph, together with analyses of the oxygen and carbon dioxid content of the venous blood in seven cases. The metabolism experiments were made with the Zuntz apparatus. One of the most striking results is the extraordinarily low value obtained in all cases for the respiratory quotient. In the two milder cases the quotients for experiments with the subjects at rest and fasting were 0.743 and 0.603, while three similar observations in the more severe case gave as respiratory quotients 0.574, 0.534 and 0.614. Exercise brought about a rise of the quotient. In the last case exhausting work raised the quotient to 0.933 and 0.923. The blood-gas analyses showed an increase over the normal carbon dioxid content of the venous blood both at rest and during work. Kraus believed that the low respiratory quotients and the high blood carbon dioxid were best explained by assuming that one of the essential factors of the dyspnea of cardiac patients is that the lung has lost its ability to excrete carbon dioxid and take up oxygen normally, either on account of a disturbance of its glandular function (Bohr), or because of pathologic changes in the lining epithelium or the pulmonary vessels.

Grafe[2] reports observations made with the "Kopfrespirationsapparat" on the metabolism of seven patients with cardiac disease. The

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1. Kraus: Die Emüdung als ein Mass der Constitution, Bibliotheca Medica, Abt. D[1], Hefte 3, Cassel, T. G. Fisher & Co., 1897.

2. Grafe: Gaswechseluntersuchungen bei fortgeschrittenen Erkrankungen der Lungen an der Zirkulationsorgane, Deutsch. Arch. f. Klin. Med., 1909, xcv, 543.

method is open to criticism. The respiratory quotient was 0.885 in a case of congenital heart disease, 0.733 in one with Pick's cirrhosis, and 0.764 in a case of arteriosclerosis with myocarditis, but in the four other cardiac patients the quotients were remarkably low: 0.638, 0.632, 0.619 and 0.586. These instances with low respiratory quotients showed comparatively normal oxygen consumption, but low carbon dioxid production. Grafe demonstrates by calculations that it is quite impossible to accept the theory of Kraus, which accounts for the low quotients on the basis of carbon dioxid retention, as the amounts of carbon dioxid stored up in the body would be too enormous. He believes that the low respiratory quotients signify a qualitatively altered metabolism with incomplete oxidations, and suggests that the accumulation of carbon dioxid, which Kraus demonstrated by blood-gas analysis, may have injured the body protoplasm so that the chemical changes pursue an abnormal course. There seemed to be no relation between respiratory rate and increase of oxygen consumption.

While some of the respiratory quotients obtained by Grafe are so low that it is almost impossible not to suspect their accuracy, nevertheless his theory as to an altered metabolism finds some confirmation in the work of other authors who have shown that acidosis is frequently associated with cardiac disease. Thus, according to Beddard and Pembrey,[3] the alveolar carbon dioxid tension is very low in cases of decompensated cardiac disease. French, Pembrey and Ryffel[4] found it low in cases of congenital heart disease with cyanosis. Fitzgerald[5] obtained normal values for the alveolar carbon dioxid in the majority of cardiac cases, but low values in a case of mitral stenosis. and extremely low figures in a case of congenital heart disease. Porges, Leimdörfer and Markovici[6] studied a considerable series of patients with heart disease, and found that in general the carbon dioxid tension of the alveolar air is normal in those which were without dyspnea, but that it tended to be below normal in the dyspneic patients. The lowest tensions in compensated patients without dyspnea occurred in two cases of congenital heart disease, both of which probably had open ductus Botalli. Lewis[7] and his associates have shown by investigations on the blood and alveolar air that the attacks of dyspnea so commonly seen in elderly patients with renal disease or advanced arteriosclerosis are accompanied by an acidosis which they believe to be the cause of the disturbance of respiration. In cases of pure valvular

3. Beddard and Pembrey: Brit. Med. Jour., 1908, ii, 580.
4. French, Pembrey and Ryffel: Jour. Physiol., 1909, xxix, Proc., p. 9.
5. Fitzgerald: Jour. Path. and Bacteriol., 1910, xiv, 328.
6. Porges, Leimdörfer and Markovici: Ztschr. f. klin. Med., 1913, lxxvii, 446.
7. Lewis, Ryffel, Wolf, Cotton and Barcroft: Heart, 1913, v, 45. Lewis and Barcroft: Quart. Jour. Med., 1915, vii, 97.

disease with cyanosis, they found no evidence of acidosis, but that there may be an acidosis in severely decompensated cases, which disappears as compensation is regained, is shown by the observations of Porges, Leimdörfer and Markovici.[6] It is, however, particularly in the type of case which may be conveniently grouped under the heading of "cardiorenal" disease that the factor of acidosis assumes a more permanent and thus a more important part. The association of acidosis with chronic nephritis has been carefully discussed by Sellards[8] and by Palmer,[9] and its relation to the course of the disease has been studied by Peabody.[10] The significance of acidosis in investigations on metabolism was first suggested by Benedict and Joslin,[11] who showed that in two normal subjects an acidosis resulting from the administration of a carbohydrate-free diet was accompanied by an increase in the total metabolism. This observation has since been confirmed by Higgins, Fitz and Peabody.[12] Lusk believes that this increase is due to the increased protein metabolism of the carbohydrate-free periods.

METHODS USED

It is thus quite evident that in studying the metabolism of patients with heart disease it is of the utmost importance to know whether or not there is an acidosis. On account of its direct bearing on the subject of acidosis, and also on account of any other possible, but as yet unknown effects which a nephritis may exert on the metabolism, it is also of importance to know as much as possible about the functional capacity of the kidneys. At the time when the earlier of the cases reported here were investigated, renal function tests were not in general use, but the later cases were, whenever possible, studied with these points in mind. As an index of acidosis, the carbon dioxid tension of the alveolar air was determined. This was done by the Higgins modification of the method of Plesch, which has proved very satisfactory for clinical work. The normal alveolar carbon dioxid tension by this method is approximately 40 to 45 mm. In some instances the alkali tolerance test of Sellards[8] was used. The determination of the part played by the kidneys in cases of cardiac or cardiorenal disease is, of course, proverbially difficult and unsatisfactory. In general we have relied on the history, physical examination, urine examination, blood

8. Sellards: Johns Hopkins Hosp. Bull., 1912, xxiii, 289; ibid., 1914, xxv, 141.
9. Palmer: Med. Communicat., Mass. Med. Soc., 1913, xxiv, 133.
10. Peabody, F. W.: Studies on Acidosis and Dyspnea in Renal and Cardiac Disease, The Archives Int. Med., 1914, xiv, 236; Clinical Studies on the Respiration, II, The Acidosis of Chronic Nephritis, ibid., 1915, xvi, 955.
11. Benedict and Joslin: Publications of the Carnegie Institution of Washington, 1912, Pub. 176.
12. Higgins, Fitz and Peabody: Unpublished.

pressure and phenolsulphonephthalein test to aid us in differentiating the pure cardiac from the renal or cardiorenal cases.

The patients were all from the medical wards of Bellevue Hospital, but during the period of study they were kept in the special metabolism ward. The general method of conducting the observations was similar to that described in the third and fourth paper of this series.[13] The patients were usually put into the calorimeter for a short period in the afternoon, in order that they might become accustomed to the new surroundings, and then put in again for the actual experiment on the following day. As one of the chief points which we wished to investigate was the influence of dyspnea on the metabolism, quite a number of the decompensated patients were put into the calorimeter. In spite of their comparatively serious condition, however, no patient was in any way injured by his stay in it. The majority said they felt better when they came out, and, indeed, the period of absolute quiet seemed to have only a beneficial effect. The construction of the chair described in the eleventh paper made it possible to study the metabolism of patients with orthopnea. The respirations were counted by watching the patient through the glass window in the side of the calorimeter, but the graphic records registered by the spirometer on a kymograph for the five minutes at the end of each period were of help, particularly in drawing attention to periodic breathing.

DISCUSSION OF RESULTS

The total number of patients investigated was sixteen. One of these (Case 3, Fred D.) was examined first when he was decompensated and dyspneic (3a), and later when he was compensated (3b). Six cases (11, William S., 12, George M., 13, Marcus R., 14, David K., 15, William A., 16, Theodore S.) were studied for purposes not directly connected with the present investigations so that the details on them are not complete, but they are included since they serve as controls of the more severely ill patients, and contribute information about various special points. Seven cases 2, Armon W., 3, Fred D., 4, Edward M., 9, Burrell P., 11, William S., 15, William A., 16, Theodore S.) were instances of pure cardiac disease; two were cases of nephritis (12, George M., 14, David K.) and six (1, Arthur V., 5, Charles L., 7, Edward W., 8, Henry R., 10, August F., 13, Marcus R.) were mixed cases belonging to the "cardiorenal disease" group. At the time when they were in the calorimeter, five patients (1, Arthur V., 3a, Fred D., 4, Edward M., 8, Henry R., 10, August F.) had moderately severe dyspnea; seven had slight dyspnea (2, Armon W., 5,

13. Gephart, F. C., and DuBois, E. F.: The Organization of a Small Metabolism Ward, The Archives Int. Med., 1915, xv, 829; The Determination of the Basal Metabolism of Normal Men and the Effect of Food, ibid., 1915, xv, 835.

TABLE 1.—SUMMARY OF CALORIMETER EXPERIMENTS; INDIRECT CALORIMETRY: AVERAGES PER HOUR

Case No. and Name	Date	Age	Sex*	Indirect Calorimetry: Average Calories per Kg.	Indirect Calorimetry: Per Sq. M., Meeh	Indirect Calorimetry: Per Cent. Divergence from Average Normal Basal, Meeh	Average per Hour: Per Sq. M., Linear Formula	Average per Hour: Per Cent. Divergence from Average Normal Basal Linear	Average Normal Basal Calories per Sq. M. per Hour: According to Meeh's Formula	Average Normal Basal Calories per Sq. M. per Hour: According to Linear Formula	Remarks
1. Arthur V.	2/12/15	40	♂	1.57	54.4	+42	58.7	+48	34.7	39.7	Restless
2. Armon W. ...	2/13/15	33	♂	1.21	38.6	+11	47.7	+19	34.7	39.7	Quiet
3. Fred D.	2/15/15	17	♂	1.51	45.1	+17	53.8	+28	38.5	42.0	Very quiet
	2/23/15	..	..	1.41	38.5	0	42.7	+ 2	38.5	42.0	Very quiet
4. Edward M. ..	2/17/15	37	♂	1.18	39.5	+15	....	....	34.7	....	Restless
5. Charles L. ...	2/19/15	54	♂	1.08	38.7	+26	....	....	30.8	....	Quiet
6. Annie T.	2/20/15	14	♀	1.75	42.2	+10 (?)	43.9	— 5 (?)	38.5 (?)	46.4 (?)	Slightly restless
7. Edward W.	2/24/15	37	♂	1.68	51.8	+49	....	....	34.7	....	Slightly restless
8. Henry R.†....	2/26/15	40	♂	1.05	36.0	+ 4	45.7†	+15†	34.7	39.7	Quiet
9. Burrell P.	3/24/15	41	♂	1.20	37.3	+ 7	48.9	+23	34.7	39.7	Restless
10. August F. ...	5/ 1/15	62	♂	1.04	31.7	+ 3	36.9	+ 5	30.8	35.2	Quiet
11. William S. ...	2/10/15	48	♂	1.06	34.3	— 2	41.7	+ 8	34.7	39.7	Fairly quiet
12. George M. ...	4/ 7/13	56	♂	1.08	33.1	+ 8	....	....	30.8	....	Restless
	4/14/13	..	..	1.01	31.7	+ 3	....	....	30.8	....	Quiet
	3/24/14	..	..	1.03	31.1	+ 1	....	....	30.8	....	Quiet
	4/ 4/14	..	..	1.06	31.0	+ 1	....	....	30.8		
13. Marcus R. ...	4/ 9/13	51	♂	1.34	43.5	+41	....	....	30.8	....	Very quiet
14. David K.	3/21/13	54	♂	1.22	39.3	+28	....	....	30.8	....	Restless
	3/24/13	..	..	1.14	37.0	+20	....	....	30.8		
15. William A. ..	1/25/15	24	♂	1.13	36.3	+ 5	39.6	0	34.7	39.7	Fairly quiet
	1/27/15	..	..	1.17	37.9	+ 9	41.2	+ 4	34.7	39.7	Quiet
16. Theodore S.	1/28/14	32	♂	1.17	37.1	+ 9	45.1	+ 4	34.7	39.7	Very quiet
	1/30/14	..	..	1.10	34.8	+ 2	38.8	— 2	34.7	39.7	Very quiet
	2/ 5/14	..	..	1.15	36.7	+ 7	39.9	0	34.7	39.7	Very quiet
	2/ 9/14	..	..	1.03	33.0	— 4	37.1	— 7	34.7	39.7	Very quiet
	2/13/14	..	..	1.13	36.4	+ 7	41.1	+ 3	34.7	39.7	Very quiet

* In this column, ♂ denotes male, and ♀ female.

† In Case 8 (Henry R.) there was some error in the measurements of the height or of the surface. The three measurements of the linear formula L, O and B added together give a total length of 150 cm. from soles of feet to suprasternal notch. His height was recorded as 153 cm. According to the linear formula measurement, his surface area was 1.968 sq. m. or only 13 per cent. below the figure of 2.215 obtained by Meeh's formula. With fat individuals of his body shape the true surface is usually about 20 per cent. below the estimate according to Meeh. This would make his surface about 1.77 sq. m. According to new height-weight chart it would be 1.78. His metabolism per square meter per hour on this new basis would be about 15 per cent. above the average, or 45.70 calories per square meter.

Charles L., 6, Annie T., 7, Edward W., 9, Burrell P., 11, William S., 13, Marcus R.), and five had normal respiration (3b, Fred D., 12, George M., 14, David K., 15, William A., 16, Theodore S.).

Respiratory Quotients.—In striking contrast to the results of Kraus and Grafe, which have been described above, all of the respiratory quotients in this series of cases fell within comparatively normal limits. Our lowest quotient was 0.73 (Case 4, Edward M.). Of the ten cases reported by Kraus and Grafe, only four had respiratory quotients equal or above our lowest figure, while in the other six the results had to be explained as being caused by a qualitative alteration in metabolism. On the basis of the respiratory quotients, as obtained by us, there is no need to assume any change in the type of metabolism from the normal. In general there is a distinct tendency for the lowest quotients to be found in the cases with most dyspnea. Five patients, classed as having moderately severe dyspnea, gave as quotients: 0.74, 0.75, 0.73, 0.75 and 0.82. In seven patients with slight dyspnea the quotients were 0.79, 0.76, 0.81, 0.79, 0.84, 0.82 and 0.78, while the patients without dyspnea showed the following quotients: 0.88, from 0.80 to 0.83, from 0.74 to 0.75, from 0.81 to 0.85 and from 0.80 to 0.85 (Table 2).

DIRECT AND INDIRECT CALORIMETRY

In the previous papers of this series the close agreement between the methods of direct and indirect calorimetry with normal subjects has been demonstrated. In disease, owing to certain technical difficulties, there is a tendency for the method of direct calorimetry to average from 1 to 2 per cent. lower, particularly if short periods are used. In the group of cardiac and nephritic patients here presented, the total of the calories measured by indirect calorimetry is 4,297.67, by direct calorimetry 4,214.53, or 1.93 per cent. lower. This is remarkably good agreement, considering the technical difficulties, and indicates that there is no profound change in the metabolism which would upset calculations based on the method of indirect calorimetry.

TOTAL METABOLISM

The total metabolism is compared with the normal in terms of the heat production per square meter of surface area per hour. After the linear formula was devised, it was possible to measure most of the patients in this manner and use the results as a basis of the calculations. In all other cases it has been necessary to use Meeh's formula, which is fairly satisfactory with these subjects, since they all happened to be of about the normal body shape.

Of the five patients with moderately severe dyspnea, all but one (Case 10, August F.) showed a distinct increase in metabolism. Of

TABLE 2.—CLINICAL FINDINGS AND—

Case No. and Name	Age	Date in Calorimeter	Diagnosis	Blood Pressure	Pulse Rate	Phthalein Per Cent.
1. Arthur V.	40	2/12/15	Chronic nephritis, chronic myocarditis with decompensation	110-70	99	2/15=32% 2/27=63%
2. Armon W.	33	2/13/15	Double mitral disease, auricular fibrillation	110-70	77	—
3a. Fred D.	17	2/15/15	Double mitral disease, decompensation	—	105	—
3b. Fred D.	..	2/23/15	Compensated	95-70	86	—
4. Edward M.	37	2/17/15	Mitral insufficiency, auricular fibrillation, decompensation	120-85	78	—
5. Charles L.	54	2/19/15	Aortic and mitral insufficiency, chronic nephritis, emphysema	180-90	71	30%
6. Annie T.	14	2/20/15	Congenital heart disease, open ventricular septum, dextrocardia	95	102	—
7. Edward W.	37	2/24/15	Chronic nephritis, cardiac dilatation, syphilis	190-100	112	10%
8. Henry R.	40	2/26/15	Chronic myocarditis, emphysema, chronic nephritis	160-120	116	48%
9. Burrell P.	41	3/24/15	Aortic stenosis and insufficiency, mitral and tricuspid insufficiency, aneurysm of aorta	—	66	—
10. August F.	62	5/ 1/15	Chronic nephritis, auricular fibrillation	170-110(?)	77	24%
11. William S.	48	2/10/15	Adherent pericardium	110-80(?)	91	—
12. George M.	56	4/ 7/13	Chronic nephritis, cardiac hypertrophy	170-95	64	....
		4/14/13	....	170-55	.....	....
		3/24/14	....	195-115	59	....
		4/ 4/14	....	160-102	60	....
13. Marcus R.	57	4/ 9/13	Chronic nephritis, mitral insufficiency, arteriosclerosis	810-160	81	....
14. David K.	54	3/21/13	Chronic nephritis, arteriosclerosis, inguinal hernia	195-110	.....	....
		3/24/13	....	....	.....	....
15. William A.	24	1/25/15	Aortic insufficiency	140	61	....
		1/27/15	....	....	66	....
16. Theodore S.	32	1/28/14	Mitral stenosis, auricular fibrillation....	....	50	....
		1/30/14	....	....	58	....
		2/ 5/14	....	....	49	....
		2/ 9/14	....	....	48	....
		2/13/14	....	145-85	55	....

—CALORIMETER RESULTS COMPARED

Arterio-sclerosis (radial)	Resp. Rate	Dyspnea	Or-thop-nea	Periodic Resp.	Cyano-sis	Edema	Alveolar CO_2 Tension, mm.	R. Q.	Metab. % Devia-tion from Av. Norm.	
0	36	+	+	+	Slight	0	2/12=23.9 2/16=30.9 2/27=41.6	0.739	+48	
0	26-28	Slight	..	0	Slight	....	2/18=44.2	0.791	+19	
0	27-25	+	+	0	Slight	+	2/15=27.8 2/16=33.7	0.758	+28	
0	22-18	0	0	0	Slight	0	2/18=35.5 2/23=37.1	0.876	+ 2	
0	30-24	+	+	0	+	Slight	2/16=38.6	0.733	+15	
0	28-26	Slight	..	+	0	0	2/19=39.4	0.766	+26	
0	20-18	+	0	0	++	0	2/18=25.2	0.807	— 5	
+	23-21	Moderate	+	+	Slight	Slight	2/24=38.9 2/27=40.0	0.789	+49	Died, April 17, 1915
0	39-38	++	+	Slightly	—	Slight	2/25=41.1 2/26=39.9	0.747	+15	
+	25-22	Slight	+	0	—	....	—	0.837	+23	
+	28-27	+	++	+	Slight	+	—	0.815	+ 5	
..	19-18	Slight	+	0	+	....	—	0.817	+ 8	
Slight	.....	Slight	....	.....	....	±	....	0.819	+ 8	
.....	.....	Slight	....	.....	....	+	....	0.796	+ 8	
.....	24-18	Slight	....	.....	....	+	....	0.827	+ 1	
.....	.....	Slight	....	.....	....	+	....	0.815	+ 1	
++	20-18	Slight	....	.....	0	0	....	0.781	+41	
+	.....	0	0	.....	0	0	....	0.746	+28	
+	.....	0	0	.....	....	....	....	0.744	+20	
.....	.....	0	0	.....	....	....	....	0.852	± 0	Lying flat on back
.....	.....	0	0	.....	....	....	....	0.814	+ 4	Steamer chair
0	.....	0	0	.....	+	0	....	0.822	+ 9	Flat on back
.....	.....	0	0	.....	+	0	....	0.831	+ 2	Sitting in bed at angle of 30°
.....	.....	0	0	.....	+	0	....	0.808	+ 7	Lying flat on back
.....	.....	0	0	.....	+	0	....	0.842	— 4	Sitting up at angle of 50°
.....	.....	0	0	.....	+	0	....	0.854	+ 7	Lying flat on back

the seven with slight dyspnea, all showed an increase except the under-developed girl with congenital heart disease. Of the five with no dyspnea, the only one with increased metabolism was the restless and unsatisfactory alcoholic, David K. (Case 14).

Dyspneic patients must do an increased amount of muscular work in their labored breathing, but it is doubtful if this would account for an increase of 10 per cent. Some of the dyspneic patients were rest-

TABLE 3.—Patients with Moderately Severe Dyspnea, Slight Dyspnea and No Dyspnea

Subject	Case No.	Pulse	R. Q.	Per Cent. Increase of Metabolism above the Normal	Alveolar CO_2 Tension, mm.
Patients with moderately severe dyspnea					
Arthur V.	1	99	0.789	+48	28.9
Fred D.	3a	105	0.758	+28	27.8
Edward M.	4	78	0.733	+15	33.6
Henry R.	8	116	0.747	+15?	39.9
August F.	10	77	0.815	+ 5	....
Patients with slight dyspnea					
Armon W.	2	77	0.791	+19	44.2
Charles L.	5	71	0.766	+26	39.4
Annie T.	6	102	0.807	— 5 ?	21.7
Edward W.	7	112	0.789	+49	38.9
Burrell P.	9	66	0.887	+23	....
William S.	11	91	0.817	+ 8	....
Marcus R.	13	81	0.781	+41	....
Patients with no dyspnea					
Fred D.*	3b	105	0.758	+ 2	37.1
George M.	12	59-64	0.80-0.83	+ 1 to + 8	....
David K.	14	.....	0.74-0.75	+20 to +28	...
William A.	15	61	0.81-0.85	0 to + 4	....
Theodore S.	16	48-55	0.80-0.85	— 7 to + 4	....

* Compensated.

less while in the calorimeter, but a similar degree of restlessness in other patients does not increase the metabolism more than about 10 per cent. This factor may be of some importance in the cases of Arthur V. (Case 1), Edward M. (Case 4), Edward W. (Case 7), Burrell P. (Case 9) and David K. (Case 14), but other patients with high metabolism for example, Armon W. (Case 2), Fred D. (Case 3), Charles L. (Case 5), Henry R. (Case 8) and Marcus R. (Case 13) were as quiet as the normal controls. It is evident that most dyspneic

patients show a metabolism increased from some cause other than muscular activity.

An analysis of the relation between increase of metabolism in these cases and acidosis is of considerable interest. It is unfortunate that the carbon dioxid tension of the alveolar air was not determined in all the patients. The lowest carbon dioxid was found in Case 6 (Annie T.), but it is quite possible that in such a case of congenital heart disease the decreased alveolar carbon dioxid might not be accurate evidence of the change in the reaction of the blood. Excluding this patient, the two with the lowest carbon dioxid, Arthur V. (Case 1) and Fred D. (Case 3) showed marked increase in metabolism. Still there were two others with high metabolism (Edward W., Case 7, and Charles L. Case 5) whose alveolar carbon dioxid was very slightly depressed.

It is interesting to note that patients with low excretion of phenolsulphonephthalein, Arthur V. (Case 1), Charles L. (Case 5) and Edward W. (Case 7), showed marked increase in metabolism; but one, August F. (Case 10), whose phenolsulphonephthalein was low, showed no increase.

Six patients gave systolic blood pressure readings of 170 mm. or over. Of these four, Charles L. (Case 5), Edward W. (Case 7), Marcus R. (Case 13) and David K. (Case 14) had high metabolism, while two, August F. (Case 10) and George M. (Case 12), had low metabolism.

It is evident that in so complex a group of subjects as the sixteen cardiacs and nephritics, there are many factors at work. At present it would seem as if no one factor would account for the definite increase in metabolism found in the dyspneic patients. The studies in this subject are being continued.

It is of interest to note that patients with compensated cardiac lesions or with mild nephritis show a metabolism within the normal limits.

SUMMARY AND CONCLUSIONS

Sixteen patients with cardiac and cardiorenal disease have been studied, and for the first time the methods of direct and indirect calorimetry have been compared. In this group of cases the two methods have been found to agree within 1.9 per cent.

The respiratory quotient in all cases was within normal limits (0.73 or above). This is opposed to the findings of Kraus and Grafe. The normal quotients and the very close agreement of the direct and indirect calorimetry prove that there is no profound change in the intermediary metabolism.

TABLE 4.—

Subject, Date, Weight, Surface Area, Linear Formula	Period	End of Period	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.
Case 1 (Arthur V.) 2/12/15	Prelim.	11:19	.....	.....	.....	.....	.....	......	.....
58.26 Kg. 1.556 Sq. M.	1*	12:22	30.05	29.35	0.75	49.92	0.331	96.62	94.96
	2†	1:19	26.41	26.26	0.73	48.47	0.331	85.99	88.82
								182.61	
Case 2 (Armon W.) 2/18/15	Prelim.	11:25	.....	.....	.....	.....	.....	......	.....
60.77 Kg. 1.550 Sq. M.	1	12:25	24.11	21.78	0.81	27.78	0.266	72.69	72.61
	2	1:25	23.85	22.87	0.78	28.82	0.266	74.15	71.81
								146.84	
Case 3 (Fred D.)... 2/15/15	Prelim.	11:34	.....	.....	.....	.....	.....	......	.....
49.75 Kg. 1.394 Sq. M.	1	12:34	28.87	22.54	0.75	36.61	0.579	73.75	76.63
	2	1:34	24.07	23.30	0.75	37.44	0.579	76.27	78.63
								150.02	
Fred D. 2/23/15	Prelim.	11:19	.....	.....	.....	.....	......	......	.....
39.68 Kg. 1.291 Sq. M.	1	12:19	19.07	14.77	0.94	24.00	0.331	50.76	56.63
	2	1:19	20.53	16.90	0.88	25.27	0.331	57.38	60.43
	3§	1:49	9.82	8.87	0.81	12.48	0.331	29.56	29.00
								137.70	
Case 4 (Edw. M.).. 2/17/15	Prelim.	11:30	.....	.....	.....	.....	.....	......	.....
68.88 Kg.	1	12:30	23.35	23.41	0.76	36.73	0.399	76.37	89.58
	2	1:30	26.87	26.37	0.74	36.51	0.399	86.49	90.02
								162.86	
Case 5 (Chas. L.) 2/19/15	Prelim.	11:25	.....	.....	.....	.....	.....	......	.....
85.84 Kg.	1	12:25	28:50	27.18	0.76	35.43	0.287	89.96	89.41
	2	1:25	30.50	28.84	0.77	39.05	0.287	95.71	93.28
								185.67	
Case 6 (Annie T.).. 2/20/15	Prelim.	10:57	.....	.....	.....	.....	.....	......	.....
26.27 Kg. 1.046 Sq. M.	1	11:57	15.29	13.69	0.81	20.09	0.150	45.83	42.82
	2	12:57	15.20	13.78	0.80	20.78	0.150	46.02	43.80
								91.85	
Case 7 (Edw. W.).. 2/24/15	Prelim.	11:18	.....	.....	.....	.....	.....	......	.....
54.85 Kg.	1	12:18	28.90	26.69	0.79	47.27	0.357	88.64	89.[illegible]
	2	1:18	30.78	28.29	0.79	47.66	0.357	94.21	94.88
								182.85	
Case 8 (Henry R.) 2/26/15	Prelim.	11:32	.....	.....	.....	.....	.....	......	.....
75.49 Kg. 1.73(?) Sq. M.	1	12:32	24.62	24.07	0.74	38.36	0.308	79.21	77.35
	2	1:32	24.75	23.98	0.75	40.81	0.308	78.91	80.88
								158.12	

* 63 min. † 57 min. § 30 min.

—Calorimeter Experiments

Direct Calorimetry (Rectal Temp.), Cal.	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M.	
......	37.61									
94.15	37.60	100	37.2	0.74	9	80	11	1.66	52.28	Restless period 68 min.
81.51	37.46	97	45.0	0.72	10	86	4	1.48	46.48	Restless period 57 min.
175.66										
......	36.99									
72.78	37.00	76	14.2	0.81	10	58	32	1.20	38.19	Quiet; reading 40 min.
71.50	37.00	78	30.8	0.77	10	71	20	1.22	38.96	Quiet; reading 5 min.
144.28										
......	38.17									
74.68	38.15	104	5.0	0.74	21	70	9	1.48	44.29	Very quiet
76.00	38.11	105	14.0	0.74	20	71	9	1.58	45.81	Very quiet
150.68										
......	36.88									
56.41	36.88	86	5.0	0.97	17	8	74	1.28	35.45	Asleep 40 min.
55.16	36.68	81	7.0	0.90	15	29	56	1.45	40.07	Very quiet
29.54	36.70	91	4.0	0.81	15	55	30	1.49	41.28	Very quiet
141.11										
......	36.99									
80.00	36.88	80	41.5	0.71	14	85	1	1.11	37.08	Very restless
92.59	36.88	76	33.0	0.73	12	81	7	1.26	42.00	Restless
172.59										
......	37.15									
86.23	37.11	70	23.6	0.76	8	75	17	1.05	37.55	Quiet, dozing and reading
96.41	37.16	71	25.0	0.77	8	72	20	1.12	39.95	Quiet, reading
182.64										
......	37.16									
42.07	37.09	102	24.0	0.81	9	59	32	1.74	42.12	Restless
44.23	37.12	102	16.0	0.80	9	62	29	1.75	42.30	Fairly quiet
86.30										
......	37.55									
80.94	37.37	111	25.0	0.79	11	66	23	1.63	50.19	Fairly quiet; dozing
97.28	37.46	112	32.0	0.79	10	64	26	1.73	53.35	Slightly restless
178.22										
......	37.40									
76.49	37.39	117	21.0	0.74	10	79	10	1.05	36.02	Quiet
75.94	37.32	115	13.0	0.74	10	79	10	1.05	35.88	Quiet
152.43										

Subject, Date, Weight, Surface Area, Linear Formula	Period	End of Period	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.
Case 9 (Burrell P.)	Prelim.	11:10	.....	.....	.....	.....	.....	......	.....
3/24/15 70.81 Kg. 1.739 Sq. M.	1	12:10	30.81	27.06	0.82	33.75	0.544	90.29	88.94
	2	1:10	27.96	23.67	0.86	29.89	0.544	79.67	86.20
								169.96	
Case 10 (Aug. F.)	Prelim.	12:00	.....	.....	.....	.....	.....	......	.....
5/1/15 52.61 Kg. 1.487 Sq. M.	1	1:00	18.26	15.49	0.86	25.98	.....	Approx. 52.50	49.62
	2	2:00	18.38	17.29	0.77	25.55	.....	57.27	51.67
								109.77	
Case 11 (Wm. S.)..	Prelim.	11:29	.....	.....	.....	.....	.....	......	.....
2/10/15 65.02 Kg. 1.62 Sq. M.	1	12:29	22.68	19.76	0.84	22.48	0.515	65.97	65.29
	2	1:29	23.75	21.83	0.80	24.97	0.515	72.40	71.41
								138.37	
Case 12 (Geo. M.)	Prelim.	10.00	.....	.....	.....	.....	.....	......	.....
4/7/18 54.29 Kg.	1	12:00	40.20	34.52	0.85	45.15	0.392	115.92	104.18
	2	2:00	38.76	35.64	0.79	49.34	0.392	118.02	115.02
								233.94	
George M.	Prelim.	10:00	.....	.....	.....	.....	.....	......	.....
4/14/18 57.18 Kg.	1	12:00	36.23	32.33	0.82	46.23	0.311	107.87	101.38
	2	2:00	39.98	37.36	0.78	49.48	0.311	123.66	112.01
								231.53	
George M.	Prelim.	11:36	.....	.....	.....	.....	.....	......	.....
3/24/14 58.82 Kg.	1	12:36	19.31	16.27	0.86	23.14	0.335	54.85	61.59
	2	1:36	20.08	18.44	0.79	25.08	0.335	61.10	65.68
								115.95	
George M.	Prelim.	11:40	.....	.....	.....	.....	.....	......	.....
4/4/14 58.98 Kg.	1	12:50	22.70	21.12	0.78	26.32	0.402	69.74	68.87
	2	1:40	16.14	18.84	0.85	18.94	0.402	46.44	46.38
								116.18	
Case 13 (Marcus R.)	Prelim.	10:00	.....	.....	.....	.....	.....	......	.....
4/9/19 68.48 Kg.	1	12:00	55.21	52.33	0.77	68.56	0.456	172.64	148.96
	2	2:00	55.27	50.59	0.80	74.22	0.456	168.03	162.08
								340.67	
Case 14 (David K.)	Prelim.	9:40	.....	.....	.....	.....	.....	......	.....
3/21/18 62.66 Kg.	1	10:40	25.86	25.55	0.74	32.26	0.323	83.84	79.94
	2	11:40	21.78	20.91	0.76	23.71	0.323	68.89	66.49
								152.73	
	3	12:40	27.18	26.95	0.73	32.44	0.323	88.36	82.37
	4	1:40	29.85	27.48	0.78	32.74	0.323	91.04	84.88
	5	2:40	25.50	23.78	0.78	30.95	0.323	78.89	80.54
	6	3:40	23.74	23.61	0.73	30.16	0.323	77.32	79.79
								488.34	

Direct Calorimetry (Rectal Temp.), Cal.	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M. (Meeh)	
......	37.37									
79.78	37.72	68	36.0	0.82	16	51	33	1.30	39.67	Restless
81.04	37.64	64	35.0	0.87	18	36	46	1.13	35.01	Restless
160.82										
......	38.18									
45.76	38.10	78	12.0	....	..	..	..	....	.....	Very quiet; asleep 15 min.
51.43	38.10	76	7.9	....	..	..	..	....	.....	Quiet
97.19										
......	36.79									
59.13	36.68	85	8.0	0.84	21	43	36	1.02	33.13	Very quiet
71.16	36.71	98	27.6	0.80	19	55	26	1.11	36.36	Restless
130.29										
......	36.52									
112.80	36.72	64	....	0.86	18	40	42	1.07	32.84	Restless
117.72	36.79	...	....	0.79	18	59	23	1.09	33.43	Restless
230.52										
......	36.78									
96.03	36.66	...	....	0.82	15	53	32	0.94	29.52	Asleep
115.88	36.76	...	....	0.77	13	67	20	1.08	33.84	Slightly restless
211.91										
......	36.68									
50.97	36.47	58	14.9	0.88	19	34	47	1.02	29.46	Asleep 30 min.
63.66	36.47	60	21.8	0.79	17	59	24	1.04	32.81	Asleep 10 min.
114.63										
......	36.53									
64.04	36.54	59	29.8	0.78	18	62	20	1.01	32.04	
50.94	36.64	60	9.0	0.86	19	39	42	0.94	29.87	
114.98										
......	37.24									
165.91	37.57	...	....	0.76	14	70	16	1.36	44.09	Very quiet
163.27	37.60	...	....	0.79	14	61	25	1.32	42.91	Very quiet
329.18										
......	36.97									
82.17	37.02	...	....	0.73	10	83	7	1.34	43.26	Restless
69.16	37.06	...	....	0.75	12	75	13	1.10	35.47	Restless
151.33										
......	37.01	...	....	0.72	10	84	6	1.41	45.49	At 11:40 a. m., oatmeal
......	36.97	...	....	0.78	9	70	21	1.45	46.87	
......	37.09	...	....	0.78	11	67	22	1.26	40.62	
......	37.01	...	....	0.72	11	84	5	1.23	39.81	
155.33										

TABLE 4.—Calorimeter—

Subject, Date, Weight, Surface Area, Linear Formula†	Period	End of Period	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.
David K. .... 3/24/13 64.26 Kg.	Prelim.	9:21	.....	.....	.....	.....	.....	......	.....
	1	10:21	22.91	22.75	0.73	27.51	0.391	74.39	68.85
	2	11:21	22.66	21.78	0.76	27.73	0.391	71.65	67.05
								146.04	
Case 15 (Wm. A.).. 1/25/15 63.44 Kg. 1.795 Sq. M.	Prelim.	11:18	.....	.....	.....	.....	.....	......	.....
	1	12:18	25.32	20.31	0.91	34.45	0.382	69.44	72.58
	2	1:18	24.06	20.86	0.84	32.15	0.382	70.14	73.06
	3	2:18	24.45	22.02	0.81	31.11	0.382	73.44	73.48
								213.02	
William A. .... 1/27/15 63.00 Kg. 1.790 Sq. M.	Prelim.	10:40	.....	.....	.....	.....	.....	......	.....
	1	11:40	24.37	21.06	0.84	32.50	0.390	70.86	73.83
	2	12:40	25.01	22.17	0.82	32.37	0.390	74.09	75.33
	3	1:40	24.75	23.05	0.78	33.58	0.390	76.88	78.06
								221.83	
Case 16 (Theo. S.) 1/28/14 59.52 Kg. 1.68 Sq. M.	Prelim.	11:10	.....	.....	.....	.....	.....	......	.....
	1	12:10	23.13	20.30	0.83	39.08	0.454	67.86	77.28
	2	1:10	23.96	21.43	0.81	38.26	0.454	71.40	76.66
								139.26	
Theodore S. .... 1/30/14 59.44 Kg. 1.68 Sq. M.	Prelim.	11:15	.....	.....	.....	.....	.....	......	.....
	1	12:15	21.66	18.76	0.84	36.00	0.385	62.97	73.11
	2	1:15	22.80	20.18	0.82	37.75	0.385	67.48	73.83
								130.45	
Theodore S. .... 2/5/14 60.28 Kg. 1.69 Sq. M.	Prelim.	11:46	.....	.....	.....	.....	.....	......	.....
	1*	1:16	34.63	31.59	0.80	50.61	0.538	105.10	113.65
	2	2:16	22.82	20.53	0.81	32.00	0.359	68.47	72.40
								173.57	
Theodore S. .... 2/9/14 61.15 Kg. 1.70 Sq. M.	Prelim.	11:50	.....	.....	.....	.....	.....	......	.....
	1	12:50	21.11	18.41	0.83	21.14	0.394	61.66	56.93
	2	1:50	22.34	19.11	0.85	22.55	0.394	64.30	60.38
								135.96	
Theodore S. .... 2/13/14 61.99 Kg. 1.71 Sq. M.	Prelim.	11:10	.....	.....	.....	.....	.....	......	.....
	1	12:10	24.54	20.49	0.87	26.73	0.391	69.38	70.40
	2	1:10	24.35	21.15	0.84	33.09	0.391	71.02	75.79
								140.40	

* 1½ hours. † In the case of Theodore S. the height-weight formula.

Direct Calorimetry (Rectal Temp.), Cal.	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M. (Meeh)	
......	36.96									
76.52	37.11	...	....	0.72	14	82	4	1.16	37.66	
66.14	37.10	...	....	0.75	14	73	13	1.11	36.27	
142.66										
......	36.96	..	....	....	..	..	..	....	.....	Basal; flat in bed
62.29	36.77	62	20.2	0.93	15	20	65	1.10	35.47	Restless
69.48	36.71	60	10.5	0.85	14	68	18	1.11	35.82	Fairly quiet
70.55	36.66	62	10.0	0.81	14	62	24	1.16	37.51	Quiet
202.32										
......	36.89	..	....	....	..	..	..	....	.....	In steamer chair
66.72	36.76	66	10.0	0.85	15	44	42	1.13	36.36	Quiet
72.33	36.71	66	10.5	0.82	14	53	33	1.18	38.01	Quiet
73.06	36.62	..	20.6	0.78	14	65	22	1.21	39.19	Fairly quiet
212.11										
......	37.14	..	....	....	..	..	..	....	.....	Basal; flat in bed
89.22	36.94	49	21.0	0.84	18	46	36	1.14	36.14	
71.30	36.93	50	23.2	0.82	17	52	31	1.19	38.08	
160.52										
......	37.10	..	....	....	..	..	..	....	.....	Sitting up with backrest at angle of about 30 deg.
70.46	37.05	53	1.9	0.85	16	44	40	1.06	33.58	
75.61	37.13	52	0.9	0.88	15	51	34	1.14	35.99	
146.07										
......	37.08	..	....	....	..	..	..	....	.....	Basal; flat in bed
86.70	36.87	50	10.0	0.80	14	60	26	1.16	37.09	
65.32	36.94	47	0.6	0.81	14	56	30	1.14	36.26	
152.02										
......	37.06	..	....	....	..	..	..	....	.....	Sitting up with backrest at angle of about 50 deg.
64.71	36.83	49	6.7	0.84	17	45	38	1.01	32.28	
67.15	36.86	46	3.7	0.86	16	40	44	1.05	33.67	
131.86										
......	37.01	..	....	....	..	..	..	....	.....	Basal; flat in bed
66.94	36.95	54	3.5	0.88	15	34	51	1.12	35.99	
75.32	36.95	55	5.5	0.84	15	45	40	1.15	36.84	
142.26										

TABLE 5.—Clinical Data

Case No., Name and Date	Total Calories	Protein, Gm.	Fat, Gm.	Carb., Gm.	Food N	Urine N	Excreta N†	N Balance	NaCl Gm.	Urine Vol., c.c.	Body Weight, Kg.
Case 15, William A. Jan. 7-8, 1915	2,753	94.1	126.0	29.15	15.05	13.86	15.37	—0.32	.....	1,255	62.88
Jan. 8-9, 1915	3,075	112.2	152.9	291.4	17.95	13.82	15.62	+2.33	.....	1,230	.....
Jan. 9-10, 1915	3,207	97.4	131.9	385.5	15.58	14.54	16.06	—0.48	.....	1,530	.....
Jan. 25-26, 1915	1,756	72.0	99.0	131.6	11.52	9.52	10.67	+0.85	.....	1,232	63.44
Jan. 26-27, 1915	2,588	76.4	102.8	321.7	12.55	.....	.....	......	.....	.....	.....
Jan. 27-28, 1915	2,068	58.8	87.1	247.4	9.32	10.30	11.23	—1.91	.....	1,135	63.00
Case 5, Charles L. Feb. 19-20, 1915	1,514	33.3	69.8	177.3	5.33	8.55	9.08	—3.75	.....	685	85.84
Case 8, Henry R. Feb. 26-27, 1915	1,035	18.2	33.1	158.8	2.91	7.12	7.41	—4.50	.....	417	74.59
Case 3, Fred D. Feb. 15-16, 1915	820	31.6	39.3	79.0	5.06	12.61	13.12	—8.06	.....	913	49.75
Feb. 16-17, 1915	514	24.5	28.0	87.6	3.92	14.28	14.67	—10.75	.....	2,350	.....
Feb. 17-18, 1915	832	35.3	39.2	78.6	5.65	11.69	12.26	—6.61	26.95	4,800	.....
Feb. 18-19, 1915	1,155	34.4	48.5	137.4	5.50	7.90	8.45	—2.95	20.48	1,880	.....
Bartolo D. Mar. 11-12, 1915	2,836	85.9	147.7	246.9	13.74	6.28	7.65	+6.09	.....	1,220	.....
Mar. 12-13, 1915	2,922	100.8	131.5	313.7	16.13	5.82	6.96	+9.17	.....	1,960	43.78
Mar. 13-14, 1915	3,498	96.9	192.1	320.6	15.50	7.17	8.72	+6.78	.....	1,820	43.88
Mar. 14-15, 1915	2,983	91.8	157.6	278.2	14.69	6.89	8.36	+6.33	.....	1,700	43.33
Mar. 15-16, 1915	2,315	78.3	119.0	216.4	12.53	6.49	7.74	+4.79	.....	1,259	41.80
Morris S. Dec. 17-18, 1914	1,930	56.6	75.0	244.2	9.06	11.69	12.60	—3.54	.....	1,775 Cal. Spec.	61.21
Dec. 11-18, 1914	558 Protein meal	62.1	11.8	47.1	9.98	6.24 Cal. Spec.	.....	......	.....	875	62.81
Case 9, Burrell P. Mar. 24-25, 1915	2,306	71.1	124.0	210.0	11.38	12.37	13.51	—2.13	.....	1,035	70.81
Case 11, William S. Feb. 10-11, 1915	1,726	40.0	95.3	164.9	6.40	10.61	11.25	—4.85	.....	2,235	65.02
Feb. 11-12, 1915	2,444	59.9	117.4	269.7	9.60	.....	.....	......	.....	1,695	.....
Case 7, Edward W. Feb. 24-25, 1915	1,423	44.2	58.8	169.6	7.07	7.26	7.98	—0.91	.....	1,254	54.35
Case 16, Theodore S. Jan. 28, 1914	2,021	88.4	94.8	189.5	14.1	.....	.....	......	.....	800+	59.55
Jan. 29, 1914	2,084	96.3	87.3	201.7	15.4	.....	.....	......	.....	1,025	60.10
Jan. 30, 1914	2,065	95.4	94.4	191.4	15.3	.....	.....	......	.....	930	59.48

† Urine N + 10% of food N

Patients with compensated cardiac lesions or with mild nephritis showed no increase in the metabolism. Of twelve patients with dyspnea, nine showed a distinct rise in metabolism, and in five of these the increase was from 25 to 50 per cent. above the average normal. Two out of the five gave evidence of marked acidosis in the low content of carbon dioxid in the alveolar air. In two others, whose metabolism was just as high, there was no significant depression of the alveolar carbon dioxid.

697 Huntington Avenue, Boston—477 First Avenue, New York.

REPORT OF CASES

Case 1.—Arthur V., aged 40, Italian, admitted Feb. 10, 1915, discharged March 3, 1915. Service of Dr. Nammack.

Diagnosis: Chronic nephritis, chronic myocarditis with decompensation.

Complaint: Dyspnea and cough.

Past History: Never sick before except for an attack of bronchitis three months ago. No history of venereal disease.

Present Illness: Has been "feeling poorly" for one month. For twelve days has had shortness of breath.

Physical Examination (February 12): The patient is a well built and fairly well developed man. Height 155 cm. Skin is slightly yellowish. Sclerae clear. He is dyspneic and orthopneic. There is a slight cyanotic tinge to his lips and ears. Respiration is rapid and shallow; rate 30. Pneumographic tracings show respiration to be periodic in type. Heart: Dulness extends from 16 cm. to the left of the midsternum in the fifth space to 5 cm. to the right in the third space. The action is regular. At the apex there is a weak first sound with a faint systolic murmur and a weak second sound. Gallop rhythm at the apex. Pulmonic second sound is louder than the aortic second sound. No murmurs at the base. Radial artery not palpable. Lungs: Slight dulness at extreme right base posteriorly. Large moist râles at both bases. Abdomen, negative. Liver: Dulness extends 3 cm. below the costal margin. Edge indistinctly felt. No edema.

Pulse: Varied in rate from 72 to 116 between February 10 and February 18.

Temperature: Between February 10 and February 18 varied between 97.8 and 101 F. except on February 13, when it reached 103 F. (rectal), February 16, when it was 102.2 F. (rectal), and February 17, when it was 102.4 F. (rectal).

Urine: February 10, specific gravity, 1.026; albumin, very faint trace. One hyaline cast.

February 14, specific gravity, 1.020; albumin, cloud. Few casts.

February 23, specific gravity, 1.020; albumin, faint trace. No casts.

Blood Pressure: February 15, systolic, 110 mm.; diastolic, 70 mm.

February 16, systolic, 120 mm.; diastolic, 75 mm.

February 24, systolic, 120 mm.; diastolic, 60 mm.

Phenolsulphonephthalein Test: February 15, first hour, 20 per cent.; second hour, 12 per cent.; total, 32 per cent.

February 27, first hour, 50 per cent.; second hour, 13 per cent.; total, 63 per cent.

March 2, 1915: Roentgenoscopy does not reveal evidence of aneurysm or dilatation of the aorta. Cardiac shadow is triangular in shape with enlargement of the right heart. Cardiophrenic angle is obtuse.

Medication: Patient was on a "soft special" diet, consisting chiefly of milk, cream, bread, butter and eggs. Strophanthin, 0.5 mg., intramuscularly, on February 10. Digitalis from February 13 to February 22, inclusive.

Diet Chart Summary

Date	Food Calories	Food N, Gm.	Urine Vol., C.c.	Urine N, Gm.
2/12/13	1,246	7.28	560	10.27

Alveolar Air (Plesch-Higgins method): February 12, 23.9 mm.; February 16, 30.8 mm.; February 27, 41.0 mm.

Electrocardiogram: February 26, "R" waves small in all leads, directed down in lead 3. "P" waves larger in all leads.

In the ten days following the observations in the calorimeter, the patient's condition showed little change. His dyspnea, though of only moderate grade while he was at rest, improved but little. Physical examination remained practically unchanged.

In calorimeter, Feb. 12, 1915, No. 189.

February 13, the dyspnea is somewhat less marked. The pulse is a little smaller and the heart action not quite so strong.

February 26, seems improved. Much less dyspneic. Pulse suggestive of a Corrigan.

Case 2.—Armon W., aged 33, pedler, born in Hungary, admitted Feb. 9, 1915, discharged Feb. 18, 1915. Service of Dr. Nammack.

Diagnosis: Mitral stenosis and insufficiency. Auricular fibrillation.

Complaint: Pain in heart and right side.

Past History: Was never sick up to six months ago. Has been in hospitals twice during last six months on account of dyspnea and swollen feet. No history of rheumatism or syphilis.

Present Illness: No improvement since discharged from Beth Israel Hospital.

Physical Examination (February 13): Patient is a fairly well built young man. Height 161 cm. Respiration, 28 per minute. Slight cyanosis. Heart dulness extends from 12 cm. to left of the midsternum in the fifth interspace to the right sternal border of the sternum. First sound at apex is loud and is followed by a rumbling systolic murmur. Second sound is loud and is followed by a rumbling diastolic murmur which extends through the short diastoles but is followed by a pause before the first sound in the longer diastoles. Both second sounds are normal at the base. Action absolutely irregular. Practically all the beats reach the wrist.

Temperature: Normal.

Pulse: From 156 to 72.

Respiration: From 26 to 28. During last three days it was from 20 to 24.

Medication: Special diet. Infusion of digitalis, every four hours from February 9 to 10.

Wassermann (Feb. 10, 1915): + + +.

Blood Pressure (February 18): Systolic, 110; diastolic, 70.

Urine: February 10, specific gravity, 1.022; albumin, 0; no casts.

February 17, specific gravity, 1.030; albumin, faint cloud; no casts.

Alveolar Air (Plesch method): February 13, carbon dioxid tension 44.2 mm.

In calorimeter Feb. 13, 1915.

Case 3.—Fred D., aged 17, clerk, admitted Feb. 13, 1915, discharged March 19, 1915. Service of Dr. Nammack.

Diagnosis: Mitral stenosis and insufficiency.

Complaint: "Shortness of breath."

Past History: First attack of rheumatism at the age of 6 years. He made a complete recovery and was well until a second attack of rheumatism at 11 years of age. Since then he has been perfectly well up to the present illness.

Present Illness: Began three weeks ago with pain in the abdomen. He stopped work for one week but after that went back to work for two weeks. During the week before admission to the hospital he was troubled with marked shortness of breath. Edema of feet began on the day before admission. He has had a cough for three days.

Physical Examination (February 16): The patient is 157 cm. tall. He is slightly cyanotic and orthopneic. No clubbing of fingers. Heart: Apex impulse is in the fifth space 9 cm. to the left of the midsternal line. Cardiac dulness extends from 12 cm. to left of midsternum in the sixth space to 5 cm. to the right in the fourth space. Action regular. At the apex the first sound is followed by a blowing systolic murmur; the second sound is distant and followed by a long rumbling murmur which extends through diastole. The pulmonic second sound is accentuated. There is a loud systolic murmur in the fourth and fifth spaces just to the left of the sternum and transmitted to the right. The lungs are negative except for scattered râles and dulness at the extreme left base. Liver not felt. Abdomen negative. Slight edema of legs.

Urine: Specific gravity, 1.030; heavy cloud of albumin; many casts.

Temperature has ranged from 100 to 102 since admission.

Pulse has varied between 96 and 112; respirations from 24 to 32.

The patient was in the calorimeter, February 15, the day preceding the foregoing physical examination, and on February 23.

February 19: The patient is now almost completely compensated at rest. Respiration less rapid and less labored. Slight cyanosis persists. Heart dulness extends from 10 cm. to the left in the fifth space to 3.5 cm. to the right in the fourth space. Action regular. Sounds and murmurs are unchanged. He has been passing large quantities of water.

Date	Food Cal.	Food N.	Urine N.	Urine NaCl	Urine Vol., C.c.
2/15-16			12.61		913
2/16-17	518	3.92	14.28		2,430
2/17-18			11.69	26.95	4,800
2/18-19	1,139	4.90	7.90	20.48	1,880

February 24: Blood pressure: systolic, 95; diastolic, 70.

February 17-24, temperature varied between 98.4 and 99.8 (rectal).

February 20: Urine: Albumin negative, no casts.

The patient was on the Karrell diet and received digitalis from February 14 to February 17, inclusive.

February 24: Blood culture sterile. Wassermann negative.

March 13: Up and about.

Alveolar Carbon Dioxid (Plesch-Higgins method): February 15, average 27.7 mm.; February 16, average 33.7 mm.; February 18, average 36.7 mm.; February 23, average 37.2 mm.

Medication: Digitalin, 10 minims every four hous (8, 12, 4) the night before going into the calorimeter (Feb. 15, 1915). Also digitalin, 10 minims, every four hours (8, 2, 6) on the day of the calorimeter (Feb. 15, 1915).

No electrocardiogram.

Case 4.—Edward M., aged 37, chauffeur, born in the United States, admitted Feb. 15, 1915, discharged Feb. 27, 1915. Service of Dr. Coleman.

Diagnosis: Mitral insufficiency and auricular fibrillation.

Complaint: Dyspnea and edema of the legs.

Family History: Negative.

Past History: Had rheumatism in 1908. The attack lasted about one year, and affected all the joints of his limbs. He was in bed off and on. Four years ago he was refused life insurance. He has had dyspnea, palpitation, edema of the feet and vertigo for several years. During the last year these symptoms have been severe. This is his third admission to the hospital since last May. No history of venereal disease.

Present Illness: Legs have been more swollen during the last week. Dyspnea and cough are more severe, so he has returned to the hospital.

Physical Examination (Feb. 17, 1915): The patient is a large, well developed man. He is orthopneic and distinctly cyanotic, but his respiration is

slower and not so labored as it was yesterday. He coughs occasionally but raises little sputum. Heart: Dulness extends from 14 cm. to the left of the midsternum in the fifth space to 4 cm. to the right in the fourth space. Pulse 86, irregular in force and rhythm. No pulse deficit. At the apex the first sound is poor in quality, and is followed by a blowing systolic murmur which is transmitted to the left. No murmurs at the base. Pulmonic second sound is louder than the aortic. Radial artery not palpable. Lungs: Slight dulness at the left base posteriorly. Numerous sibilant and sonorous râles throughout the chest. Liver: Edge indistinctly made out 5 cm. below the costal margin in the right mammary line. No fluid in the abdomen. Slight edema of the back and legs.

Pulse, between February 16 and February 20, ranged from 56 to 108. It was 120 once, and 140 once.

Temperature reached 102 F. (rectal), February 16. From then to February 20 it was below 99.8 F. (rectal).

Respiration varied from 24 to 30 on the first three days in the hospital, and was subsequently 20 or less.

Blood Pressure: February 16, systolic, 120; diastolic, 85.

Urine: February 16, specific gravity, 1.025; trace of albumin; no casts.

Medication: Soft diet. Digitalis from February 16 to February 19, infusion of digitalis, 20 minims, the night before and on the day he was in the calorimeter.

Alveolar Air (Plesch method): February 16, carbon dioxid tension, 38.3 mm.

Electrocardiogram shows auricular fibrillation. "T" waves directed down in the second and third leads.

Patient regained compensation rapidly, and on February 24 was beginning to get up in a chair.

In calorimeter, Feb. 17, 1915.

Discharged, Feb. 27, 1915. General condition very good. Cyanosis much improved. Walks around without shortness of breath. Pulse still irregular.

Case 5.—Charles L., aged 54, laborer, born in the United States, admitted February 16, 1915, discharged Feb. 24, 1915. Service of Dr. Lambert.

Diagnosis: Chronic nephritis with hypertension. Cardiac hypertrophy with aortic insufficiency and mitral insufficiency. Emphysema.

Complaint: Shortness of breath.

Family History: Negative.

Past History: Three years ago he was sick for nine weeks with rheumatism. He had erysipelas following a fracture of the skull six years ago. He drinks a considerable amount of beer. There is no history of syphilis.

Present Illness: He has noticed dyspnea for about a month when he went upstairs. For two weeks this has been much worse and he has been unable to sleep at night.

Physical Examination (February 19): The patient is a rather large, strong man. His skin has slight yellowish tinge. Lips and mucous membranes are of fair color. There is no definite cyanosis. Respiration is quiet but somewhat rapid. Respiration is periodic in type, but without intervals of complete apnea. The chest is large, almost barrel-shaped. Heart: Dulness extends from 14 cm. in the fifth space to the left of the midsternum to the right sternal margin. No area of absolute cardiac dulness. Action regular. At the apex the first sound is rather faint and it is followed by a blowing systolic murmur. The second sound at the apex is also faint; it is followed by a blowing diastolic murmur. Both systolic and diastolic murmurs are well heard in the axilla and over the precordium. They are also audible in the first and second spaces to the right of the sternum. The murmurs are loudest in the first space to the right and in the second space to the left of the sternum. The pulse is of good size, high tension, and distinctly collapsing in type. Artery wall not palpable. Lungs: Emphysematous. Scattered râles in both sides of back. Fairly frequent cough, but little expectoration. Dulness with absent breath sounds at extreme right base posteriorly. Abdomen negative except for slight tenderness in region of the liver. Liver not felt. No edema.

Temperature: Varied between 98 and 100 F. (rectal).

Pulse: Varied between 64 and 100.

Respiration: Ran between 28 and 36 on the first two days—later between 20 and 28.

Wassermann Reaction: Negative.

Blood Pressure: February 17, systolic, 180; diastolic, 90.

Phenolsulphonephthalein Test: February 20, first hour, 10 per cent.; second hour, 20 per cent.; total, 30 per cent.

Urine: February 16, specific gravity, 1.020; albumin, heavy cloud; many casts. February 21, specific gravity, 1.018; albumin, strong trace; many casts.

Summary of Diet Chart

Date	Food Cal.	Food N.	Urine Vol., C.c.	Urine N.	Urine NaCl
2/19-20	1,524	5.82	685	8.55	12.17

Medication: Special diet. Restricted fluids. Infusion of digitalis every four hours from February 18 to February 20. Infusion of digitalis just before going into calorimeter.

Alveolar Air (Plesch method): February 19, carbon dioxid tension, 39.4 mm. at 3:30 p. m.

In calorimeter, Feb. 19, 1915.

Case 6.—Annie T., aged 14, born in the United States, admitted Jan. 14, 1915, discharged March 25, 1915. Service of Dr. Lambert.

Diagnosis: Congenital heart disease. Open ventricular septum. Dextrocardia.

Complaint: Heart trouble, headache and trembling.

Family History: Negative.

Past History: Negative except for the dyspnea associated with her cardiac condition.

Present Illness: Comes to hospital on account of a severe attack of headache, with palpitation of the heart, and stomach ache. Has had similar attacks before.

Physical Examination: Height 137 cm. The patient is a small, rather underdeveloped girl, dull mentally. She lies flat on her back breathing quietly but slightly rapidly. There is a high degree of cyanosis of lips, tongue, nose, hands and feet. There is marked clubbing of the fingers and toes. The chest is asymmetrical. Right side more prominent than left. Heart: Apex impulse is in the fifth space 9 cm. to the right of the midsternal line. The dulness extends from 11 cm. to the right in the fifth space to 4 cm. to the left of the midsternum in the fourth space. No thrills are felt. At the apex, just below and outside the right nipple, the first sound is scarcely audible, and there is a loud blowing systolic murmur. The second sound is weak. There is a loud systolic murmur heard all over the precordium and to the left of the sternum. Its maximum intensity is in the fifth space just to the right of the sternum. There is a loud, low pitched systolic murmur in the second space just to the left of the sternum, and also in the second space to the right of the sternum. Lungs: Negative on auscultation and percussion. Abdomen, liver and spleen negative. Skin harsh and dry.

Roentgenoscopy reveals transposition of heart and colon. Stomach and liver are in normal position.

Temperature: Ranges between 98.4 and 101 F. (rectal).

Pulse: Usually varies between 86 and 108.

Respiration: Now from 20 to 24.

Blood Pressure: January 27, systolic, 95 mm.

Urine: January 15, specific gravity, 1.025; albumin, cloud; granular casts.

Alveolar Air (Plesch method): February 18, carbon dioxid tension, 25.2 mm. at 4 p. m.

Blood: Jan. 28, 1915, leukocytes, 14,000; polymorphonuclears, 63; transitionals, 1; lymphocytes, 28; large mononuclears, 8; mast cells, 0.

Feb. 9, 1915, leukocytes, 15,200; polymorphonuclears, 56; transitionals, 4; lymphocytes, 28; large mononuclears, 7; mast cells, 5.

Electrocardiogram, Jan. 16, 1915, shows an inverted "T" wave in the first lead; very large "P" and "T" waves in the second lead, and very large "P" and "T" waves in the last lead, with a splitting of the "T" waves.

Electrocardiogram: Jan. 19, 1915, right and left arm terminals were normal. Shows right heart preponderance; inverted "P" and very large "T" waves in Lead 1; "P-R" interval prolonged.

In calorimeter, Feb. 20, 1915.

CASE 7.—Edward W., aged 37, born in the United States, bath attendant, admitted Feb. 22, 1915, discharged March 7, 1915. Service of Dr. Meara.

Diagnosis: Chronic interstitial nephritis. Cardiac dilatation.

Complaint: Shortness of breath; swelling of feet.

Past History: Has had frequent attacks of sore throat. Syphilis twelve years ago. Has been a heavy drinker during the last three months.

Present Illness: Five days before admission he began to be troubled with palpitation and dyspnea on exertion. Dyspnea has been much worse at night. Edema of feet for the last few days.

Physical Examination (February 24): The patient is a fairly well developed young man. His lips, ears and finger tips are slightly dusky. Definite exophthalmos. Thyroid not enlarged. Respiration is periodic, but without intervals of complete apnea. Breath urinous. Orthopnea marked. Patient says he is breathing much more easily than during the night. Heart: Dulness extends from 11 cm. to the left of the midsternum in the fifth space to 3.5 cm. to the right of the midsternum in the fourth space. At the apex the first sound is loud, followed by a soft, blowing systolic murmur and a ringing second sound. Aortic second is ringing but not accentuated. Gallop rhythm is heard all over the precordium, most marked just below the left nipple. Pulse is regular; high tension. Wall of radial artery is easily palpable. Vessels tortuous. Lungs: Negative except for scattered râles, which are most numerous at the left base. Abdomen negative. Liver negative. Very slight edema of the dependent parts of the thighs.

Pulse: From February 22 to February 25, has averaged from 86 to 116 per minute.

Respirations: From February 22 to February 25, have averaged from 20 to 32 per minute.

Temperature: From February 22 to February 25, has varied from 98.4 to 99.8 F. (rectal).

Blood Pressure: February 23, systolic, 190; diastolic, 100 mm.

Urine: February 23, specific gravity, 1.018; albumin, + + +; no casts seen.

Medication: Soft diet. Tincture of digitalis, 15 minims, every four hours from February 22 to 28.

SUMMARY OF DIET CHART

Date	Food Cal.	Food N.	Urine Vol., C.c.	Urine N.
2/24-25	1,226	3.36	1,254	7.26

Alveolar Air (Plesch method): February 24, carbon dioxid tension, 38.9 mm.

Wassermann, Feb. 28, 1915, positive, 17 units.

Alkali Tolerance Test: After 20 gm. sodium bicarbonate, given in 5 gm. doses every hour, the urine became neutral. After 25 gm. it was still neutral. Not tested later.

Phenolsulphonephthalein Test: February 27, first hour, 6 per cent.; second hour, 4 per cent.; total, 10 per cent.

February 27: The patient has Cheyne-Stokes respiration—periods of apnea and periods of intense dyspnea. He is very uncomfortable with his breathlessness. His condition appears to be much worse.

In calorimeter, Feb. 24, 1915.

March 7, 1915: Patient has improved very little. Fairly comfortable during the day, but each night suffers from shortness of breath and great restlessness. Heart action is rapid, and there is a gallop rhythm in spite of digitalis. Respiration is of Cheyne-Stokes type. Left hospital against advice in a serious condition. Died April 17, 1915.

Case 8.—Henry R., aged 40, born in the United States, waiter, admitted to hospital, Jan. 22, 1915, died March 20, 1915. Necropsy not obtained. Service of Dr. Nammack.

Diagnosis: Chronic myocarditis. Emphysema. Chronic nephritis (?).

Complaint: Shortness of breath.

Past History: Syphilis three years ago. Was in Bellevue Hospital in May, 1914, with lobar pneumonia. Has been in hospital since then with diagnosis of chronic myocarditis the first time, and chronic cardiac valvular disease the second time. Drinks two or three whiskies a day.

Present Illness: Comes into the hospital again because of increase of dyspnea since catching cold. On admission the clinical picture was that of an acutely decompensated heart. February 6, he began to run an irregular temperature, reaching sometimes 103, rectal. The diagnosis of bronchopneumonia was considered. February 21, the temperature fell to normal. Since then the highest temperature has been 101, rectal. General condition has not improved essentially.

Physical Examination (February 26): The patient is a big strong negro 153 cm. tall. Respiration is very rapid and shallow; rate, 40. There is orthopnea. Tongue and conjunctiva are rather pale. Eyes are prominent. Chest is very large. Heart: Dulness extends from 12.5 cm. to the left of the midsternum in the fifth space to 3 cm. to the right in the fourth space. The action is regular and rapid. Sounds are of fair quality. No murmurs are heard. There is a well marked protodiastolic gallop rhythm, heard best just below and outside the left nipple. Aortic second sound is slightly accentuated and ringing. Pulse is of fair quality; rate, 116 per minute. Artery wall not palpable. Lungs: Marked emphysema. Slight dulness at extreme right base posteriorly. A few scattered râles throughout both lungs. Many moist râles at the right base behind. Abdomen, negative. Liver: Edge easily felt about 3 cm. below the costal margin in the right nipple line. Slight tenderness over the liver. Very slight edema of the feet and lower legs.

Urine: Clear, amber, 1.022 specific gravity, acid, heavy cloud of albumin, many hyaline and coarsely granular casts, many leukocytes.

Blood Pressure: February 18, systolic, 138; diastolic, 105.

February 27, systolic, 160; diastolic, 120.

Phenolsulphonephthalein: Feb. 27, 1915, first hour, 30 per cent.; second hour, 18 per cent.; total, 48 per cent.

Wassermann, January 30, double positive, 12 units.

Alveolar Air (Plesch-Higgins method): February 25, carbon dioxid tension, 41.1 mm. at 5 p. m. February 26, carbon dioxid tension, 39.9 mm. at 4:30 p. m.

Medication: Soft diet. Morphin. Infusion of digitalis. Tincture digitalis. Codein ¼ grain, the night before and the morning before going into calorimeter.

Temperature: January 22 to Jan. 28, 1915, 99 to 101. January 28 to Feb. 1, 1915, 99. February 2 to Feb. 7, 1915, rose to 103.5 once. February 8 to Feb. 12, 1915, 100 to 101.5. February 12 to Feb. 16, 1915, 100 to 104. Remainder of time, 99 to 101.

In calorimeter, Feb. 26, 1915.

Case 9.—Burrell P., aged 41, laborer, admitted March 18, 1915, discharged April 5, 1915. Service of Dr. Nammack.

Diagnoses: Aortic regurgitation and stenosis. Mitral regurgitation. Tricuspid regurgitation. Aneurysmal dilatation of the aorta.

Chief Complaint: Shortness of breath.

Past History: Measles and whooping cough as child. Pneumonia twenty years ago.

Present Illness: Duration for past year. Ten weeks ago found that he could not work properly on account of shortness of breath. Has had hoarseness and sore throat. Nocturia rather frequent. Occasional headaches. Marked dyspnea, especially after work. Has had no swelling of ankles or legs at any time. Coughs frequently and has marked night sweats.

Physical Examination (March 23, 1915): Patient is a dark negro of muscular development. Is 169 cm. (5 feet 7 inches) tall. Orthopneic and dyspneic, breathing 26 to the minute. Not prostrated nor in much distress. An occasional unproductive cough. Heart: Apex beat in sixth space, 15 cm. to the left. Action is regular, not rapid; forceful. At the apex there is a blowing systolic murmur transmitted to the left, and a waterfall, diminuendo diastolic murmur heard with maximum intensity to the left of the sternum, but audible over the whole precordium. In the third left space there is a short presystolic murmur (Flint?). Over the aortic region there is a harsh systolic and a soft diastolic murmur. Pulse: Large excursion, quick rise and fall. Artery wall moderately thickened. Lungs: No dulness; many sibilant and sonorous râles. Cervical, axillary, epitrochlear, inguinal glands considerably enlarged.

March 19, 1915: Electrocardiogram shows a large "P" wave and the "T" wave is directed upward in each lead. There is marked left sided preponderance.

April 1, 1915: Some dyspnea. Complains of precordial pain. Heart not much changed.

Urine: Negative.

Blood: No data.

Temperature ran to 101.5 F., March 18, 1915; below 100 F. the rest of the time.

Pulse: March 18, 1915, from 104 to 112; March 19, 1915, from 70 to 80.

Respiration: March 18, 1915, from 20 to 32.

In the calorimeter, March 24, 1915.

March 18, 1915: Pupils unequal. React sluggishly. Aortic arch is dilated and heart is greatly enlarged down and to the left, also to the right of the midsternal line. Systolic thrill palpable over the aortic area. Apical impulse is forceful. Systolic and diastolic murmur is heard at the apex. Aortic second sound is accentuated. A systolic murmur is heard over the tricuspid area. There is an extracardiac sound heard which appears to be a pericardial rub. The pulse is of a typical Corrigan type.

March 22, 1915: Condition improved. Rhythm regular. Rate slow. Pericardial scratch persists. Seems much better compensated.

Medication: Digitalin, 15 minims, every four hours, the day before going into the calorimeter. Also ¼ grain codein, the night before going into the calorimeter.

Case 10.—August F., aged 62, tailor, married, admitted April 26, 1915, died May 20, 1915.

Diagnosis: Chronic interstitial nephritis and auricular fibrillation.

Complaint: Shortness of breath. Swelling of feet. Pain in chest.

Past History: There is a family history of cardiac disease. He was told that he had albumin in the urine many years ago. He had pneumonia long ago. Has had no rheumatism. Three months ago fluid was removed from his chest.

Present Illness: Began three years ago with a feeling of fatigue and shortness of breath. He has had remissions ever since. Also occasional headaches and night sweats. He feels very weak.

Physical Examination: The patient is 159 cm. tall. He is very orthopneic and in considerable distress. His lips are dry and cyanotic. Teeth are bad.

There are many râles over both bases of the lungs. Heart: Right border 3 cm. from the midsternal line. Upper border at the third rib. Left border 14 cm. and the apex 13 cm. from the midsternal line. There is a faint systolic blow heard over the apex. The sounds are of poor muscular quality. There is a harsh systolic murmur heard over the aortic area. The pulse is somewhat irregular. Walls palpable.

April 27: Pulse slower after strophanthin and digitalis.

April 29: A rough, hard systolic murmur is heard over the base of the heart, loudest in the third left space. The second sound is also loudest in this site. There is a moderate amount of fluid in the abdomen. Edema of the extremities.

May 1: Dulness at both bases posteriorly. Breath sounds diminished in intensity at the bases, where one hears an occasional râle. The cardiac impulse is less pronounced than on admission. The heart is still much dilated. There is a rough blow at the mitral area. The aortic second sound is slightly prolonged. The heart impulse is in the fifth space, 12 cm. to the left of the midline. The left limit of dulness is in the sixth space, 12.5 cm. to the left of the midline. Right limit of dulness is in the fourth space, 4 cm. to the right of the midline. There is a systolic murmur of maximum intensity to the right of the sternum. The patient has very scant beard. Pubic hair of female type. The patient is very orthopneic: distinctly dyspneic and shows marked Cheyne-Stokes breathing when asleep or quiet. He is slightly cyanotic. There is distinct edema of the flanks and legs. The breath is slightly urinous.

Urine: Cloudy, amber colored, specific gravity, 1.010, trace of albumin, hyaline and granular casts, leukocytes, erythrocytes.

Blood Pressure: Systolic, 170; diastolic, 110 (?), May 1, 1915.

Blood: Leukocytes, 15,600; polymorphonuclears, 68 per cent.; transitionals, 3 per cent.; lymphocytes, 25 per cent.; large mononuclears, 4 per cent.

Temperature: April 27 to May 12, from normal to 100; May 13 to May 19, 103.

Respiration: During high temperature, from 24 to 32.

Pulse: During high temperature, from 104 to 120.

Electrocardiogram: May 3, shows auricular fibrillation and left hypertrophy.

Phenolsulphonephthalein Test: May 8, first hour, 13 per cent.; second hour, 11 per cent.; total, 24 per cent.

The patient grew more and more orthopneic and dyspneic until death. Breath became more urinous.

Case 11.—William S., aged 48, longshoreman, admitted Dec. 22, 1914, discharged March 1, 1915. Service of Dr. Coleman.

Diagnosis: Adherent pericardium and auricular fibrillation.

Complaint: Shortness of breath. Pain in lumbar region.

Past History: Healthy until 1913, when he had pneumonia and was in Ward B2 of the Bellevue Hospital. After discharge he was weak and dyspneic for two months and was unable to work. Since then he has had a productive cough. He has lost weight and has had hemoptysis. There is a positive history of syphilis and gonorrhea.

Present Illness: Dec. 22, 1914, while unloading heavy lumber, he became suddenly short of breath. He rested but obtained no relief.

Physical Examination: The patient is 171 cm. tall, a moderately well nourished man, propped up in bed, markedly dyspneic and somewhat cyanotic. Pupils are sluggish. He is breathing rapidly and shallowly. There is diffuse systolic impulse over a broad area at the apex. The area of absolute cardiac dulness is very much enlarged. The sounds are of poor quality. There are no murmurs. The abdomen is distended and somewhat tender. The liver is felt at the umbilicus. Heart: Right border is 10 cm. to the right of the midline; left border, 14 cm. to the left of the midline. A triangular area of dulness.

Wassermann: Anticomplementary.

Jan. 2, 1915: General condition much improved. Broadbent's sign present.

Jan. 27, 1915: Patient sat up for two hours without any ill effect.

Feb. 3, 1915: Three days ago the patient developed shortness of breath; precordial pain; edema of the extremities.

Feb. 10, 1915: Dyspnea less marked. Cyanosis persists. Heart action very irregular, sounds faint, no distinct murmurs. Regurgitant wave in the jugulars. Few moist râles at bases.

Feb. 28, 1915: Distention of abdomen relieved by catharsis. Dyspnea continues. Heart irregular. Condition improved slightly.

Urine: Dec. 23, 1914, clear, pale amber, specific gravity 1.020, acid, faint trace of albumin, few hyaline casts.

Blood: Dec. 24, 1914, leukocytes, 4,800; polymorphonuclears, 73 per cent.; transitionals, 5 per cent.; lymphocytes, 12 per cent.; large mononuclears, 8 per cent.; eosinophils, 1 per cent.

Temperature: December 23 to December 25, from 101 to 103 F. December 26 to Feb. 28, 1915, from normal to 99 F.

Pulse: In the beginning from 100 to 146; later, from 60 to 80; then from 80 to 95.

Respiration: In the beginning, from 28 to 36; later, from 24 to 28.

Blood Pressure: Dec. 26, 1914, systolic, 110; diastolic, 80 (?).

Electrocardiogram: December 28, auricular fibrillation; "T" waves directed down in all leads.

Roentgenoscopy: December 30, moderate enlargement to the right and left; marked irregularity in the outline of the right diaphragm suggesting extensive adhesions.

In calorimeter, Feb. 10, 1915.

Case 12.—George M., aged 56, saloonkeeper, watchman, porter, admitted Jan. 19, 1914, discharged April 29, 1914. Service of Dr. Meara.

Diagnosis: Chronic interstitial nephritis and cardiac hypertrophy.

Complaint: Shortness of breath. Swelling of the feet.

Past History: Alcoholic. Had measles when a child. Gonorrhea thirty-four years ago.

Present Illness: In December, 1911, he first noticed shortness of breath on exertion and swelling of feet after work. Had to stop work about the 10th of June, 1911, because of the shortness of breath and edema of feet. His abdomen then began to increase in size and he became yellowish in color. His scrotum and penis began to swell. Frequent micturition. Oct. 23, 1912, he was taken with shortness of breath again, cough and swelling of the legs. Aug. 5, 1913, his legs began to swell, and he became very dyspneic on walking. His sputum became bloody. He could not lie down in bed on account of dyspnea. His abdomen increased in size.

Physical Examination (Jan. 19, 1914): The patient is a well nourished man propped up in bed showing considerable dyspnea. His face is flushed and somewhat edematous. Chest symmetrical and emphysematous. Sibilant and sonorous râles anteriorly and posteriorly. Heart: Right border 7 cm. to the right; left border 13 cm. to the left; cardiac impulse 12.5 cm. from the midsternal line. It extends to the third rib above. The sounds at the apex are of poor muscular quality. There are extrasystoles, some of which are not felt at the wrist. At the base the sounds are distant. No murmurs can be definitely made out. The pulse is irregular in force and rhythm. The vessel walls are slightly thickened. Liver dulness extends 2 cm. below the costal margin. Extremities edematous.

Jan. 22, 1914: Left lung shows dulness to flatness from the angle of the scapular to the base with a pleuritic rub. Heart: Left border 13 cm. from the midsternal line in the fourth-fifth interspace; right border 7 cm. from the midsternal line in the third-fourth interspace. Extends to third rib above.

Feb. 23, 1914: Doing well. No edema. Heart regular. Patient has a pulsus alternans.

March 14, 1914: Looks very well. On sodium chlorid has incomplete elimination with formation of an edema and increased blood pressure. On potassium chlorid the elimination is complete, associated with diuresis and fall of blood pressure.

April 28, 1914: General condition excellent. Heart as noticed above. Discharged.

Urine: Nov. 10, 1912, cloudy, amber, specific gravity 1.022, acid, faint trace of albumin, finely granular casts, leukocytes +, erythrocytes +.

Blood: Dec. 6, 1912, leukocytes, 11,000; polymorphonuclears, 73 per cent.; transitionals, 7 per cent.; lymphocytes, 15 per cent.; large mononuclears, 8 per cent.; hemoglobin, 90 per cent.; reds, 4,504,000.

Blood Pressure: March 24, 1914, systolic, 195; diastolic, 115. April 4, 1914, systolic, 160; diastolic, 102.

Pulse: March 24, 1914, from 72 to 90; April 4, 1914, from 72 to 80.

Respiration: March 24, 1914, from 18 to 24; April 4, 1914, from 20 to 24.

Temperature: March 24, 1914, subnormal; April 4, 1914, subnormal.

Wassermann: Dec. 8, 1913, positive.

Phenolsulphonephthalein: Jan. 27, 1914, 55 per cent. in two hours.

Case 13.—Marcus R., aged 51, Hebrew, tinsmith, admitted March 10, 1913, discharged April 12, 1913. Service of Dr. Thompson.

Diagnosis: Chronic interstitial nephritis, arteriosclerosis, mitral insufficiency.

Past History: He had malaria at the age of 17 to 20 years. Had pneumonia in 1877. He is a moderate user of alcohol; occasionally took whisky before breakfast.

Present Illness: In January, 1912, his legs began to swell. Since then he has been short of breath and has not been able to walk. He has been very thirsty and gets up once or twice at night to pass water. Three weeks ago he caught cold.

Physical Examination: The patient is of medium stature and heavy build. He is slightly dyspneic. The apex is in the fifth space, 14 cm. from the midline. The sounds are booming. There is a loud systolic murmur at the apex. The aortic second sound is very much accentuated. The artery wall is very thick, and there is a question of calcification. Tension is high. Pulse is regular. Many crackling and moist râles over the lungs. Liver edge is felt one hand's breadth below the costal margin. The surface is hard and nodular. There is shifting fluid in the flanks.

Urine: March 10, from 600 to 1,400 c.c.

Blood Pressure: March 10, systolic, from 300 to 320; diastolic, from 140 to 180. March 16-31, systolic, 300 to 310; diastolic, 115 to 150. April 1-9, systolic, 300 to 320; diastolic, 150 to 170.

Temperature: March 10, from 98 to 100 F. March 16-31, normal. April 1-9, normal.

Pulse: March 10, from 88 to 100. March 16-31, 72 to 80. April 1-9, 78 to 84.

Respiration: March 10, from 20 to 30. March 16-31, 18 to 20. April 1-9, 18 to 20.

Weight: March 10, 149½ pounds. March 16-31, from 140 to 137 pounds.

Case 14.—David K., aged 54, architect in reduced circumstances, admitted Feb. 21, 1913, discharged March 26, 1913. Service of Dr. Hartwell.

Diagnosis: Chronic interstitial nephritis. Arteriosclerosis. Inguinal hernia.

Past History: Three years previous to admission he noticed a small lump in his left groin. There was little discomfort until two years later when it became painful. Is very alcoholic.

March 21, 1913: Four weeks ago the patient was operated on for inguinal hernia. He now seems absolutely normal. He was out on a pass yesterday and returned at 7 p. m. For breakfast he had a cup of coffee without sugar or milk.

March 26, 1913: Heart: apex neither visible nor palpable. Left limit of dulness in the fifth space, 12.5 cm. to the left of the midline. Over the aortic area there is a rough systolic impurity of the first sound. The second aortic sound is loud and ringing. There is no enlargement to the right of the sternum. The radials are palpable.

March 26, 1913: Patient discharged.

Urine: Trace albumin.

Blood Pressure: March 26, systolic, 195; diastolic, 110.

Case 15.—William A., aged 24, laborer, admitted Dec. 28, 1914, discharged Jan. 30, 1915. Service of Dr. Coleman.

Diagnosis: Aortic regurgitation.

Complaint: Pain in right side of chest. Difficulty of breathing when lying down.

Past History: Has had measles, pneumonia and rheumatism. Has had gonorrhea. Tonsils have given him trouble. Tonsils are enlarged.

Present Illness: Dec. 25, 1914, he was taken with a very sharp pain in his side. The following night he could not lie down. He felt his heart beating. He now feels weak and coughs a good deal.

Physical Examination: The patient is a well developed and well nourished young man 180 cm. tall. His tonsils are swollen and congested. The cardiac impulse is seen in a diffuse area around the nipple and is forcible. The upper border is in the third interspace; right border 4 cm. from the midsternal line; left border 13 cm. from the midsternal line. There is a Flint murmur at the apex, and also a diastolic murmur. Corrigan pulse.

January 11, 1915: Lungs are normal. Patient is comfortable except for a slight cough. The diastolic and Flint murmurs still continued. There is a short systolic murmur at the apex.

January 15: There is a blowing systolic murmur at the aortic region, transmitted along the vessels of the neck and arm.

January 26: The patient has been in a chair all day without fatigue. He was examined upright in the chair. The cardiac impulse was forceful, maximum in the fifth space. The left limit of dulness in the fifth space, 13.5 cm. from the midline, in the fourth space 11.5 cm. from the midline; right limit of dulness at the sternal margin. In the aortic region there is a systolic murmur transmitted upward and a blowing diastolic murmur transmitted downward. At the apex there is a short systolic murmur and a rumbling murmur in diastole. Pulse of Corrigan type.

Blood Pressure: Systolic 140.

Urine: Clear, amber, specific gravity 1.030.

Temperature: Dec. 31, 1914, to Jan. 2, 1915, from 99 to 101 F. Jan. 6, 1915, varied slightly around the normal.

Respiration: From 18 to 20.

Pulse: From 65 to 80.

Electrocardiogram: "T" waves directed downward in the second and third leads. In the calorimeter, Jan. 25 and 27, 1915.

Case 16.—Theodore S., aged 32, coachman, single, admitted Jan. 17, 1914, discharged Feb. 22, 1914.

Diagnosis: Chronic cardiac valvular disease. Cardiac hypertrophy and dilatation.

Past History: He had pneumonia at the age of 6 years. In 1906 he had typhoid fever. He has had no rheumatism. At 8 years of age he was operated on for some abdominal condition. He was a moderate user of beer, but for the last two or three years he has used none. He stopped working one year ago. In Sweden he did rough carpenter work one year. Last year he was a driver.

Present Illness: For four or five years he has been short of breath, especially on exertion. At times he has had a pain in his left side. For one month he has had a short, sharp, hacking cough. He sleeps well. He was obliged to take an

easy job three years ago, as the doctor said he had heart trouble. Eight months ago he could carry a trunk upstairs. For two weeks he has been confined to the house.

Physical Examination: The patient is of medium build, 169 cm. tall, a well developed and well nourished man. Arteries are palpable. Sibilant râles at both bases.

Jan. 19, 1914: Patient is quite comfortable, not dyspneic, slight cyanosis of the lips.

January 26: Condition excellent. Slight cough, no dyspnea, no orthopnea. Sat up in chair without fatigue. Apex beat in the fifth space, 12 cm. from the midline; left limit of dulness in the fifth space 14.5 cm. from the midline, in the fourth space 12.5 cm. from the midline; right limit of dulness in the third space 3 cm. from the midline, in the fourth space 4 cm. from the midline. Heart action very slow, heavy, irregular in force and rate. Tracings show absence of the "A' wave, typical auricular fibrillation. At the apex the first sound is sharp and short. The second sound is faint. There is a loud, rough, rumbling murmur starting almost immediately after the second sound and diminishing in intensity during diastole, lasting throughout the short diastolic pauses, but stopping before the end of the long diastoles. At the base of the heart the pulmonic second sound is very much accentuated. The radial pulse corresponds with the apex impulse. The beats vary in size. Wall not palpable. There are a few sibilant and sonorous sounds in the lungs. No edema. Mucous membranes are deep red and slightly cyanotic.

February 10: The patient is up and about. He can walk up one and a half flights of steps.

February 11: The patient was given 1/120 grain atrophin, repeated after twenty-one minutes. Five minutes after the second dose the pulse rate increased from 48 to 55; the apex rate increased up to 96, and there was a large pulse deficit. At the apex the rate became almost regular, but not so regular in force. Throt dry, pupils dilated. The patient felt bad the next day, "As if he had been on a debauch."

February 15: The patient is sitting in a chair. Pulse 49; blood pressure, large beats, systolic, 145; diastolic, 85. After climbing stairs, pulse, 46, diastolic blood pressure, 150; systolic, 85.

February 21: Sounds as before. Wassermann negative.

Temperature: January 17-27, from 98 to 100 F. From January 28 on, the temperature was normal.

Roentgenogram of heart:

	Upright	Horizontal
Left	11.3	12.85
Right	8.35	7.8
	19.65	20.65

No medication.

The patient caught cold at home and was readmitted, March 4, 1914, with bronchopneumonia. Heart sounds the same. Discharged March 27, 1914.

CLINICAL CALORIMETRY

SEVENTEENTH PAPER

METABOLISM AND TREATMENT IN DIABETES *

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The experiments here to be described concern two patients with moderate diabetes treated by the oatmeal method in the metabolism ward of the Russell Sage Institute of Pathology and four Rockefeller Hospital patients with more severe diabetes transferred to Bellevue Hospital for study in the respiration calorimeter during various stages of the fasting treatment. Only very brief mention is possible of the literature[1] concerning the subjects touched upon in the experiments, namely, (1) the oatmeal and fasting treatment, (2) the dextrose-nitrogen ratio, (3) the respiratory quotient under certain conditions, and (4) the total metabolism in diabetes.

1. According to literature previously reviewed,[2] the von Noorden school no longer holds that oatmeal stands entirely alone in respect to the capability of utilization by diabetic patients, but nevertheless maintains that for some unknown reason it is superior to other forms of carbohydrate. On the other hand, Blum[3] and a series of later authors have been able to observe no difference in the clinical effects of oatmeal and other carbohydrates. Also von Noorden has claimed that cases of the worst type are the ones that do best on oatmeal, whereas in mild cases the method often fails. The opposing authors found that oatmeal, like other carbohydrates, was tolerated better in mild cases and worse in severe cases. Furthermore, even in the seemingly favorable cases where the carbohydrate balance is strongly positive, respiration experiments have usually shown little or no combus-

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1. A fuller review by one of the authors (F. M. A.) is to be published elsewhere.

2. Allen, Frederick M.: Studies Concerning Glycosuria and Diabetes, Harvard University Press, Cambridge, Mass., 1913.

3. Blum, L.: Les Hydrates de Carbone dans le Traitement du Diabete Sucré, Semaine Médicale, 1911, xxxi, 313; Ueber Weizenmehlkuren bei Diabetes mellitus, Beitrag zur Theorie der Verwendung der Kohlehydrate in der Therapie der Zuckerkrankheit, München. med. Wchnschr., 1911, lviii, 1433; Die Diät bei Diabetes gravis, Med. Klin., 1913, p. 702.

tion of carbohydrate. Thus Benedict and Joslin[4] concluded that the carbohydrate ingested produced no material effect upon the metabolism; and Joslin[5] shows the failure of either oatmeal or potato to raise the respiratory quotient, notwithstanding positive carbohydrate balances as high as 100 gm. Falta[6] states, without giving details, that a diabetic patient taking 400 gm. oatmeal daily without glycosuria showed no rise in the respiratory quotient on the first or second days, but on the third day a marked rise in the quotient occurred. Normal persons showed the usual prompt rise in the quotient; but when subjected to the customary program of the "oat cure," namely, first a period of carbohydrate-free diet, then the customary fasting or vegetable-day, then a period of 400 gm. oatmeal daily, a normal person showed the same behavior as the diabetic, in that the quotient rose only on the third day. The reason was believed to be that the organism, impoverished in carbohydrate, first stored the ingested starch as glycogen without burning any considerable quantity. The records of Rolly[7] and Roth[8] concerning the administration of different carbohydrates to diabetics show no appreciable changes in the quotients during the series of successive days in their experiments. Joslin[5] pointed out that the respiratory quotient of Benedict's fasting man rose promptly on taking mixed diet at the end of a thirty-one-day fast. Confirmation is necessary before it can be accepted that either a diabetic or a normal subject will store the carbohydrate of 400 gm. oatmeal for two days, and then suddenly show active combustion on the third day. Any such change in the respiratory quotient of a diabetic patient would more probably indicate an improvement in the power of carbohydrate combustion.

Von Noorden and all other writers admit that many cases of diabetes are so severe that neither the glycosuria nor the acidosis is cleared up by the oatmeal treatment. The method recently introduced,[9]

4. Benedict, F. G., and Joslin, E. P.: Metabolism in Diabetes Mellitus, Carnegie Institution of Washington, 1910, Pub. No. 136, pp. 203, 215; A Study of Metabolism in Severe Diabetes, Carnegie Institution of Washington, 1912, Pub. No. 176; Ueber den Stoff- und Energieumsatz bei Diabetes, Deutsch. Arch. f. klin. Med., 1913, cxi, 333.

5. Joslin, E. P.: Carbohydrate Utilization in Diabetes, The Archives Int. Med., 1915, xvi, 693.

6. Falta, W.: Zur Theorie und Behandlung des Diabetes mellitus, Med. Klin., 1914, x, 9.

7. Rolly, F.: Zur Theorie und Therapie des Diabetes mellitus, Deutsch. Arch. f. klin. Med., 1912, cv, 494.

8. Roth, N.: Ueber Mehltage bei Diabetes, Wien. klin. Wchnschr., 1912, xxv, p. 1864.

9. Allen, Frederick M.: Studies Concerning Diabetes, Jour. Am. Med. Assn., 1914, lxiii, 939; Boston Med. and Surg. Jour., 1915, clxxii, 242; New York State Jour. Med., 1915, xv, 330; Am. Jour. Med. Sc., 1915, cl, 480; Exercise, Boston Med. and Surg. Jour., 1915, clxxiii, 743; Investigative and Scientific Phases of the Diabetic Question, with Their Probable Relations to Practical Problems of Clinical Medicine, Jour. Am. Med. Assn., 1916, lxvi, No. 20, p. 1525.

consisting of a prolonged initial fast with subsequent strict regulation of all elements of the diet, has proved successful in clearing up both the urinary and the clinical symptoms in a considerable number of cases, even of very severe diabetes. The underlying principles will be discussed more fully elsewhere, but one feature considered theoretically important for the beneficial results has consisted in a diminution in the metabolism, not merely of the sugar-forming materials (carbohydrate and protein) but also of fat. The question of diminution of metabolism could be settled only by experiments in the respiration calorimeter.

2. The first dextrose-nitrogen ratio was established by Minkowski, who discovered that totally depancreatized dogs, fasting or on carbohydrate-free diet, excreted in the urine approximately 2.8 gm. of glucose for each gram of nitrogen. A constant ratio at this level indicates that 45 per cent. of the protein catabolized is being formed into glucose and excreted, and that no sugar is being formed from fat. The original interpretation was furthermore that 45 per cent. represents the maximum proportion of protein convertible into sugar. Lusk[10] and collaborators demonstrated that phlorhizinized dogs eliminate approximately 3.65 gm. of glucose for each gram of nitrogen, thus proving that at least some species of animals are capable of converting nearly 60 per cent. of the protein molecule into glucose. Also, there is no formation of sugar from fat under these conditions. Mandel and Lusk[11] demonstrated the 3.65 ratio in a human patient with severe diabetes. They urged the prognostic value of determinations of the relations of sugar and nitrogen on carbohydrate-free diet; and because the total loss of power to use carbohydrate indicated by the 3.65 ratio supposedly precluded improvement, they referred to this as the "fatal ratio." Foster and Greenwald[12] also described cases showing this ratio. For other literature, reference may be made to Lusk.[13] Inasmuch as the case described by Allard showed a fall in the ratio on fast-days, Lusk considered it no longer certain that the 3.65 ratio is necessarily permanent or fatal.

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10. Lusk, G.: Phlorhizinglukosurie, Ergebnisse der Physiologie, 1912, xii, 315.

11. Mandel, A. R., and Lusk, G.: Stoffwechselbeobachtungen an einem Falle von Diabetes mellitus, mit besonderer Berücksichtigung der Prognose, Deutsch. Arch. f. klin. Med., 1904, lxxxi, 472; Diabetes Mellitus. Report on a Case, Including a New Method of Prognosis, Jour. Am. Med. Assn., July 23, 1904, p. 241.

12. Foster, N. B.: Wie hoch ist der Dextrose: Stickstoff-Quotient bei schwerstem Diabetes? Deutsch. Arch. f. klin. Med., 1913, cx, 501; Greenwald, I.: Jour. Biol Chem., 1913-14, xvi, 375; and 1914, xviii, 115.

13. Lusk, G.: Metabolism in Diabetes, The Archives Int. Med., 1909, iii, v; Note on "A Case of Pancreatic Diabetes Mellitus," by Herman O. Mosenthal, The Archives Int. Med., 1912, x, 122. Allard: Arch. f. exper. Path. u. Phar., 1907, lvii, 1.

3. The level of the respiratory quotient theoretically to be expected in diabetes has been discussed by Magnus-Levy[14] and by Lusk.[15, 16] On the basis of the newer information concerning the amino-acid content of proteins, the latter calculates that when the dextrose-nitrogen ratio is 3.65, the quotient of protein is 0.632. The formation and excretion of acetone bodies also tends to lower the quotient in a manner which can be calculated; but at the same time such acid substances may react with sodium bicarbonate to set free carbon dioxid, so that the precise theoretical value of the quotient in diabetes cannot be determined. The actual observations in phlorhizinized dogs and human patients with the 3.65 ratio are found to meet the theoretical expectations with quotients approximating 0.69. Two features of the recent literature concerning the respiratory quotient require mention in the present connection. One is the absence, in exact modern work, of the very low quotients previously found in diabetes and other conditions. Leimdörfer[17] is the only recent author who reports such low quotients; and as they are so numerous in his experiments, while his cases of diabetes were obviously of no extraordinary severity, it is apparent that something in his methods tended to give low values. Grafe and Wolf,[37] though reporting dextrose-nitrogen ratios indicating formation of sugar from fat, found no support for this hypothesis in the respiratory quotient, which was about 0.74. Technical errors, especially in connection with the oxygen measurements (Benedict[18]), may be assumed to explain the low values in the early literature. The average quotient of Benedict and Joslin's severe cases of diabetes was 0.73; and Joslin[5] presents a table of the other cases in the literature, showing the general average to be 0.73. Respiration experiments therefore stand opposed to the doctrine of sugar-formation from fat in human

14. Magnus-Levy, A.: Respirationsversuche an diabetischen Menschen, Ztschr. f. klin. Med., 1905, lvi, 83.

15. Lusk, G.: Clinical Calorimetry, Paper Eight. On the Diabetic Respiratory Quotient, The Archives Int. Med., 1915, xv, 939.

16. Williams, H. B., Riche, J. A., and Lusk, G.: Animal Calorimetry II. The Metabolism of the Dog Following the Ingestion of Meat in Large Quantities, Jour. Biol. Chem., 1912, xii, 349, 356.

17. Leimdörfer, A.: Ueber den respiratorischen Stoffwechsel des Diabetikers bei verschiedener Kostform, Biochem. Ztschr., 1912, xl, 326.

18. Benedict, F. G.: A Comparison of the Direct and Indirect Determination of Oxygen Consumed by Man, Am. Jour. Physiol., 1910, xxvi, 15; Factors Affecting Basal Metabolism, Jour. Biol. Chem., 1915, xx, 263; Metabolism During Inanition, Harvey Lectures, 1906-07.

Benedict, F. G., and Emmes, L. E.: The Basal Gaseous Metabolism in Men and Women, Jour. Biol. Chem., 1914, xviii, 139; A Comparison of the Basal Metabolism of Normal Men and Women., Proc. Nat. Acad. Sc., 1915, i, 104; A Comparison of the Basal Metabolism of Normal Men and Women, Jour. Biol. Chem., 1915, xx, 253; Benedict, F. G., and Smith, H. M.: The Metabolism of Athletes as Compared with Normal Individuals of Similar Height and Weight, Jour. Biol. Chem., 1915, xx, 243.

diabetes. The second feature to be mentioned consists in the unexpectedly high quotients shown by some cases of severe diabetes, as observed independently by Benedict and Joslin and by observers in the Russell Sage laboratory. Table 5 in the paper by Joslin[19] contains the record of a patient with severe diabetes, fasting except for from 2 to 5 gm. protein and from 15 to 24 gm. alcohol daily, yet with respiratory quotient of from 0.74 to 0.76. Joslin[19] mentions other observations of a rise in the respiratory quotient of severely diabetic patients during fasting, even up to the neighborhood of 0.8. The cause of such high quotients is not known. Nothing analogous has been described in the study by Benedict[20] and earlier workers of cases of prolonged fasting; they found that in normal persons the quotient falls and remains low during fasting. Aside from the presumably scanty supply of stored carbohydrate, Joslin has suggested the acetone bodies as the only known material capable of raising the quotients of diabetic patients by combustion under these conditions.

4. The total metabolism in diabetes has been an actively discussed subject. The earlier literature is critically reviewed by Benedict and Joslin.[4] It has been universally agreed that the basal metabolism of mild cases of diabetes is normal, and that of most severe cases is found increased when reckoned per kilogram of body weight. But in addition to accuracy in measuring the gas exchange and heat production, there is the further requirement of an accurate basis of comparison between diabetics and other persons. Magnus-Levy[14] called attention to the fact that the emaciation of most patients with severe diabetes alters the relation of their body weight and surface, and suggested that it might be more nearly correct to compare on the basis of the original normal weight of the diabetics. Benedict and Joslin rejected this proposal, because the surface of the diabetic apparently diminishes with the body mass and the skin shows no tendency to fall in folds or wrinkles. They chose, as the most accurate means available, to compare groups of patients with severe diabetes with groups of normal and mildly diabetic persons, as nearly like them as possible in size and figure. On this basis they estimated that their severely diabetic patients showed an increase of from 6 to 7 per cent. in carbon dioxid excretion, of from 16 to 21 per cent. in oxygen consumption, and of about 15 per cent. in heat production. Lusk[21] criticized the findings in various particulars, and by recalculation concluded that the metabolism

19. Joslin, E. P.: Present-Day Treatment and Prognosis in Diabetes, Am. Jour. Med. Sc., 1915, cl, 485.
20. Benedict, F. G.: The Influence of Inanition on Metabolism, Carnegie Institution of Washington, 1907. A Study of Prolonged Fasting, Carnegie Institution of Washington, Pub. No. 203, 1915.
21. Lusk, G.: Science, 1911, N. S., xxxiii, 433-434.

represented was not 15 per cent. but only 5 per cent. above normal. Benedict and Joslin[4] in their second publication added to the number of diabetics and especially of control subjects studied, and reckoned that the basal metabolism in this group of diabetics was approximately 20 per cent. above normal. Lusk[22] calculated that an increase of from 5 to 10 per cent., and in exceptional instances 15 per cent., above normal was shown. Leimdörfer[17] found an increase of metabolism in severe cases of diabetes on the basis both of the weight and of the body surface as figured by Meeh's[23] formula. Diminution of metabolism observed after oat or vegetable days was held to confirm this interpretation. Rolly[7] found in severe diabetes an increased oxygen consumption per kilogram of body weight, especially soon after admission to hospital; after a period of treatment the findings were lower. Seib[24] also reported the respiratory metabolism increased in proportion to the severity of the case. In Paper 10 of the present series is described the height-weight formula for calculating the body surface, which has been found more accurate and reliable for this purpose than the Meeh formula, especially when the body form varies in any way from the average normal. It is possible by this formula to recalculate any results recorded in the literature, wherever the height and weight of the subject have been given. It is believed that the second of the requirements mentioned is thus fulfilled, and that, granting accurate experimental observations, a correct basis of comparison is afforded between diabetic and other subjects in a manner not possible heretofore.

The causes of the departure of the diabetic basal metabolism from the normal are partly known, perhaps partly unknown. It may be taken as an axiom that the diabetic, excreting sugar formed from protein, must catabolize more protein during fasting than the nondiabetic person under identical conditions, and that the specific dynamic action of protein will therefore give rise to a higher metabolism in the diabetic, unless some other factor prevents or neutralizes the effect of the protein. The suggestion was offered by Benedict and Joslin that acidosis may be a cause of increased metabolism. They observed the discrepant fact that a sudden slight acidosis is accompanied by an increase of metabolism out of proportion to that noted with prolonged high acidosis. At the present time the subject of acidosis is a confused one;

22. Lusk, G.: Animal Calorimetry XI. An Investigation into the Cause of the Specific Dynamic Action of the Foodstuffs, Jour. Biol. Chem., 1915, xx, 555.

23. Meeh, K.: Oberflächenmessungen des menschenlichen Körpers, Ztschr. f. Biol., 1879, xv, 425.

24. Seib, K.: Experimentelle Untersuchungen über den respiratorischen Gaswechsel bei Diabetes mellitus nach Eiweisszufuhr und bei Hyperthermie, Zentralbl. f. Physiol., 1913-14, xxvii, 930.

it can no longer be regarded as a simple condition resulting from lack of carbohydrate.[9] Greater clearness concerning the effect upon metabolism may now result from separate consideration of individual factors present. First, some or all cases of sudden acidosis are accompanied by increased protein breakdown, which may be a cause of increased metabolism. Second, if acidosis in the strict sense increases metabolism, not only should subjects with high acidosis show higher metabolism than those with low acidosis, but also alkali given in sufficient quantity should in suitable cases cause a fall in metabolism. Third, it is possible that acetone bodies, even in the form of neutral salts, may stimulate metabolism if present in excess in the blood and tissues. Here the suggestion is analogous to that of Lusk[25] that diabetic lipemia may be a cause of increased metabolism. Increased concentration of combustible materials may be expected to result in a stimulation of metabolism, unless the power of combustion is diminished, or the specific dynamic action otherwise prevented. At the same time, the narcotic and depressant action of the acetone bodies might conceivably tend to depress metabolism, especially in the long-standing cases with high ketonemia. Other influences unquestionably tend to depress metabolism in such cases, as for example undernutrition and muscular relaxation. The effect of muscular mass and tone is evident in the higher metabolism of men as compared with women, and of athletes as compared with other men (Benedict[18] and collaborators); and Lusk[22] has shown that mere prolonged cage life may reduce a dog's basal metabolism by 16 per cent., though the diet and weight remain the same. The subject will be further considered below.

An account of the metabolism in a case of diabetes of remarkable intensity was recently published by Geyelin and DuBois.[26] To facilitate reference, some of the findings in this case are briefly reproduced in Table 1.

METHODS AND CALCULATIONS

The procedures used for the chemical determinations were as follows: for the blood-sugar, the method of Lewis and Benedict;[27] for the urinary sugar, titration with Benedict's solution; for nitrogen, the usual Kjeldahl method; for ammonia, the Folin method; for acetone bodies, the Shaffer method. Foods were weighed raw and the composition estimated from the Atwater-Benedict tables, unless special mention is made of analyses. For separating the twenty-four-hour urines,

25. Lusk, G.: The Influence of Food on Metabolism, Proc. Am. Soc. Biol. Chem., December, 1914; Jour. Biol. Chem., 1915, xx, 8.

26. Geyelin, H. R., and Du Bois, E. F.: Jour. Am. Med. Assn., 1916, lxvi, No. 20, 1532.

27. Lewis, R. C., and Benedict, S. R.: A Method for the Estimation of Sugar in Small Quantities of Blood, Jour. Biol. Chem., 1915, xx, 61.

TABLE 1.—THE CASE OF CYRIL K. (SUMMARY FROM GEYELIN AND DUBOIS)

Date	Food				Urine				Respiratory Quotient	Calories per Sq. M. per Hour Linear Formula	Blood	
	Total Calories	Fat, Gm.	Nitrogen, Gm.	Carbohydrate, Gm.	Nitrogen, Gm.	Glucose, Gm.	Dextrose-Nitrogen Ratio	Beta-oxy-butyric, Gm.			Glucose, Mg. per 100 c.c.	CO_2 Combining Capacity, mm.
Dec. 8-9	438*	0	0	0	27.9	74.9	2.68	43.8	.....	....	313	30.4
Dec. 9-10	336*	0	0	0	29.8	78.3	2.61	34.6	.....	....	...	....
Dec. 10-11	0	0	0	0	24.8	74.2	2.95	....	.....	....	340	26.6
Dec. 11-12	405	17.7	2.8	41.5	30.6	108.0	2.17	60.0	.....	....	312	21.1
Dec. 12-13	1,058	69.6	8.0	50.0	34.5	112.0	1.80	53.0	.....	....	...	22.7
Dec. 13-14	938	58.5	8.8	50.0	35.4	118.7	1.63	57.9	.....	....	...	22.5
Dec. 14-15	936	51.2	9.8	53.3	37.7	118.5	1.73	55.2	.....	....	...	....
Dec. 15-16	934	41.0	19.0	23.5	36.4	167.9	3.97	70.9	0.687	45.7†	...	20.0
Dec. 16-17	458	5.6	15.9	0.4	38.3	153.4	4.01	75.1	0.714	42.6†	...	19.6
Dec. 17-18	191	2.9	6.3	0.4	36.3	140.3	3.87	87.4	.....	....	...	.... 35.4
Dec. 18-19	0	0	0	0	20.0	55.1	2.76	58.5	0.707	40.8	150	55.4
Dec. 19-20	0	0	0	0	16.7	44.3	2.65	56.8	.....	....	...	49.7
Dec. 20-21	36	0	1.6	1.0	14.1	35.3	2.44	41.2	0.721	37.0	177	52.5
Dec. 21-22	60	0	3.2	1.6	14.4	39.7	2.65	26.2	.....	....	170	....
Dec. 22-23	80	0.1	3.4	5.6	18.3	26.0	1.12	11.0	0.734	35.9	181	52.9
Feb. 16	.....	....	....	....	....	0	0	0	0.915	25.4	...	....

* Alcohol. † After breakfast, not basal.

patients emptied the bladder at precisely 5 a. m. daily, and care was taken that no urine was lost under any conditions. The entire planning and organization of the ward was for the purpose of exact metabolic studies, and accuracy in matters of dietary control, collection of excreta and other details is fully assured.

At the time of the diabetes experiments the calorimeter was in perfect working order and the staff was well trained. Alcohol checks lasting two or three hours gave respiratory quotients in which even the third decimal place was not far from the theoretical. In experiments on man it has never before been felt advisable in this laboratory to print more than two significant figures in the respiratory quotients, but it has seemed justifiable to use three in the present work, both on account of the extreme care in the experiments and of the importance of the third decimal point in some of the calculations. In no case are deductions made from single hours but only from the averages of periods as long as possible.

The calculations concerning the metabolism where there was sugar formation from protein followed the method described by Lusk.[16] In the normal metabolism each gram of nitrogen in the urine indicates the combustion of 6.25 gm. protein with the liberation from this protein of 26.51 calories, 9.35 gm. carbon dioxid and the absorption of 8.45 gm. oxygen. It is obvious that if part of this protein molecule is unoxidized in the diabetic organism and is excreted in the urine, all of these figures will be lowered by exactly the number of calories and grams of carbon dioxid and oxygen lost in the glucose. With a dextrose-nitrogen ratio of 3.65 to 1, 1 gram of nitrogen in the urine indicates the combustion of 6.25 gm. protein with the liberation of 26.51 minus 13.47 calories, 9.35 minus 5.35 gm. carbon dioxid, and the absorption of 8.45 minus 3.89 gm. oxygen. When the dextrose-nitrogen ratio is lower, the calculation is easily made as follows: The calories, carbon dioxid and oxygen ascribed to the metabolism of protein are calculated from the number of grams of nitrogen excreted per hour by using the normal factors given by Lusk.[16] Knowing the number of grams of glucose excreted per hour, one can make the proper subtractions, since each gram of glucose represents a loss of 3.692 calories, 1.467 gm. carbon dioxid and 1.067 gm. oxygen. In this way it is possible to determine the nonprotein respiratory quotient and the heat production by the method of indirect calorimetry. If there is no glycosuria, or if the sugar of the urine is all derived from ingested carbohydrate, the calculations are exactly the same as for normal persons. No attempt has been made to calculate the combustion of the acetone bodies or the ingested alcohol, the conditions of experimentation rendering this impossible.

For reasons fully stated in previous papers, the method of indirect calorimetry is used as the standard, and the divergence of the direct calorimetry from this is expressed in terms of percentage. In typhoid fever, exophthalmic goiter, anemia and cardiorenal disease there is a tendency for the direct calorimetry to average from 2 to 3 per cent. lower, probably on account of heat lost through the warming of the bed and clothing, possibly also because of errors in measuring the average temperature of the body. This same tendency to a small minus error is seen in most of the diabetes experiments. The total divergence of the two methods in the present work is 2.3 per cent., and the average

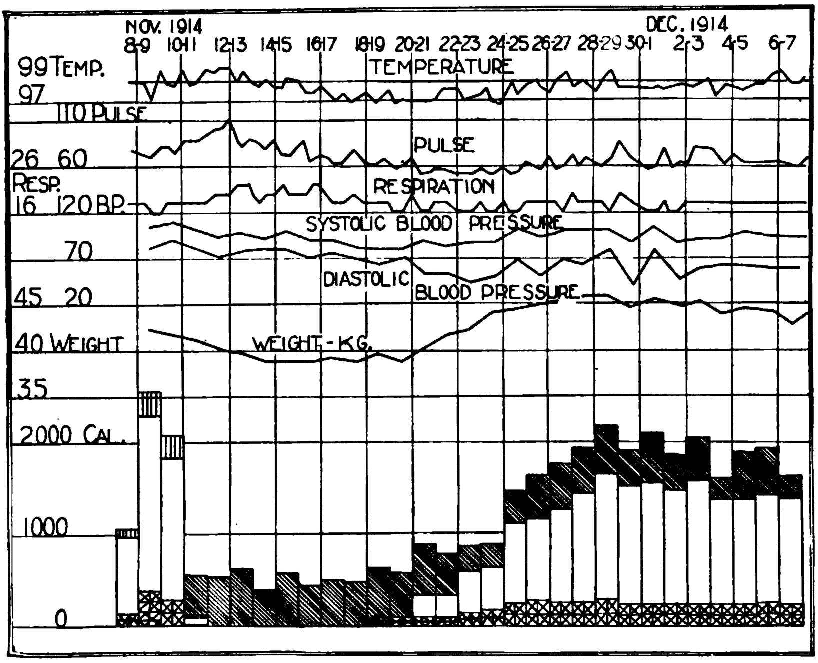

Fig. 1 (Gerald S.).—Clinical findings shown graphically. The columns at the base represent the calories of the food; vertical lines, carbohydrate; crossed lines, protein; diagonal lines, alcohol; blank space, fat calories.

divergence in individual experiments is plus or minus 5.5 per cent. The agreement of the two methods is therefore satisfactory, and would be still closer but for the peculiar divergence of the findings in the case of Gerald S. on the last day of the prolonged fast and during the following two weeks. This point is discussed in the history of his case, which follows.

CASE REPORTS

CASE 1.—Gerald S. (severe diabetes), plumber, aged 17, unmarried. Healthy family and past life, habits good, normal weight 60 kg. Polyuria and polydipsia were noticed January, 1914. Entered Bellevue Hospital June, 1914, weighing

TABLE 2.—GERALD S.:—

Date, 1914	Food						Urine N, Gm.	Urine Glucose, Gm.
	Total Calories	Protein, Gm.	Fat, Gm.	Carbo., Gm.	Alcohol, Gm.	Food N, Gm.		
Nov. 8- 9	1,056*	31.2	91.7	18.3	....	4.99	.....	.....
Nov. 9-10	2,550	96.2	204.4	62.2	....	15.40	.....	.....
Nov. 10-11	2,078	67.0	166.4	62.1	....	10.72	14.71	106.43
Nov. 11-12	540	1.3	9.5	2.3	62.6	0.20	10.76	41.95
Nov. 12-13	526	0	0	0	75.2	0	10.40	24.49
Nov. 13-14	614	0	0	0	87.7	0	10.87	15.68
Nov. 14-15	380	0	0	0	54.3	0	9.30	8.91
Nov. 15-16	555	0	0	0	79.3	0	11.10	6.53
Nov. 16-17	438	0	0	0	62.6	0	8.52	7.10
Nov. 17-18	497	0	0	0	71.0	0	8.24	2.80
Nov. 18-19	468	0	0	0	66.8	0	6.11	0.76
Nov. 19-20	622	12.2	1.8	2	79.3	1.95	7.12	0
Nov. 20-21	578	14.5	2.4	2	71.0	2.32	5.72	0
Nov. 21-22	892	24.1	25.8	2	79.3	3.85	8.41	0
Nov. 22-23	787	21.0	25.1	2	66.8	3.36	6.45	0
Nov. 23-24	878	34.6	47.7	2	41.8	5.53	9.13	0
Nov. 24-25	887	37.6	50.5	2	37.6	6.01	7.23	0
Nov. 25-26	1,464	57.9	95.9	3	50.1	9.26	6.56	0
Nov. 26-27	1,635	65.7	95.6	2	71.0	10.51	8.20	0
Nov. 27-28	1,752	61.1	110.8	2	71.0	9.77	7.17	0
Nov. 28-29	1,929	61.1	130.0	2	71.0	9.77	7.18	Trace
Nos. 29-30	2.175	68.4	151.5	2	75.0	10.75	8.58	Trace
Nov. 30-Dec. 1	1,795	56.0	140.6	2	41.8	8.96	6.89	Trace
Dec. 1- 2	2,077	55.1	146.7	2	75.2	8.81	6.73	1.71
Dec. 2- 3	1,845	57.3	138.9	2	50.1	9.16	5.72	0
Dec. 3- 4	2,034	55.7	148.1	2	66.8	8.91	5.94	Trace
Dec. 4- 5	1.606	53.9	126.6	2	33.4	8.62	5.49	0
Dec. 5- 6	1,893	53.4	126.2	2	75.2	8.54	7.23	0
Dec. 6- 7	1,942	56.9	130.0	2	75.2	9.10	6.30	0
Dec. 7- 8	1,614	54.4	127.2	2	33.4	8.70	6.61	0
Dec. 8- 9	1,872	56.4	128.9	2	66.8	9.02	6.95	0
Dec. 9-10	2,022	56.2	146.6	2	66.8	8.99	6.56	0
Dec. 10-11	2,111	54.8	145.9	2	66.8	8.76	7.28	0
Dec. 11-12	2,191	52.9	166.0	2	66.8	8.46	7.06	0
Dec. 12-13	2,308	60.0	175.6	2	66.8	9.60	7.73	0
Dec. 13-14	2,208	61.1	164.3	2	66.8	9.77	7.17	0
Dec. 14-15	2,221	59.2	166.6	2	66.8	9.74	6.22	0
Dec. 15-16	2,368	68.4	172.1	2	75.2	10.94	7.45	0
Dec. 16-17	2,582*	46.4	211.9	2	58.5	7.49	.....	.....

* Not complete.

—Clinical Data

Urine NH_3, Gm.	Beta-oxy-butyric, Gm.	Total Acetone Bodies as Beta-oxybutyric Gm.	Feces N,† Gm.	Excreta N, Gm.	Nitrogen Balance, Gm.	Water Intake, Gm.	Urine Volume, c.c.	Body Weight, c.c.	Blood Sugar, Per Cent.
....	.....	......	.....	.....	....	1,450	1,300	.....	.....
?	.....	......	.....	.....	....	2,220	?	42.19	.....
3.40	7.128	13.218	.....	15.78	— 1.07	2,960	3,526	.....	.....
4.75	2.071	3.811	0	10.76	—10.75	3,705	3,460	41.27	0.305
4.46	1.815	2.517	0	10.40	....	2,398	1,909	40.15	.....
3.08	0.594	0.990	0	.....	....	2,065	2.700	39.86	.....
2.18	0.616	1.048	0	.....	....	2,197	1,836	38.97	... ..
1.50	0.475	1.155	0	.....	....	2,450	2,563	38.92	0.286
0.90	0.416	0.656	0	.....	....	1,570	1,428	38.80	.....
0.71	0.308	0.588	0	.....	....	2,385	2,128	39.05	0.284
0.60	0.064	0.164	0	.....	....	1,725	1,153	38.74	.....
0.57	0.436	0.592	0.234	7.35	....	2,685	3,115	39.55	0.198
0.42	0.186	0.322	0.29	6.01	....	2,185	1.980	38.74	.....
0.51	0.208	0.373	0.46	8.87	....	2,883	2,360	40.22	.....
0.48	0.341	0.613	0.40	6.85	....	2,375	1,940	41.87	0.156
0.49	Lost	.....	0.66	9.79	....	2,235	1.648	42.66	.....
0.56	0.258	0.428	0.72	7.95	....	1,500	1,835	44.02	0.182
0.44	0.250	0.358	1.11	7.49	+ 1.77	1,550	1,200	44.14	.....
0.68	.....	.....	1.11	9.31	+ 1.20	2,500	3.540	.....	.....
0.46	.....	.....	1.11	8.28	+ 1.49	2,450	3,220	45.15	.....
0.50	.....	.....	1.11	8.29	+ 1.48	2,175	2,955	45.64	0.161
0.58	.....	.....	1.11	9.69	+ 1.06	2,780	4,005	45.27	.....
0.46	.....	.....	1.11	8.00	+ 0.96	1,870	2,225	44.27	.....
0.32	.....	.....	1.11	7.84	+ 0.97	1,795	3,085	45.35	0.208
0.38	.....	.....	0.945	6.67	+ 2.49	2,100	2,478	44.76	.....
0.55	.....	.....	0.945	6.885	+ 2.025	2,500	3,815	45.42	.....
0.30	.....	.....	0.945	6.435	+ 2.185	2,050	3,178	43.94	.....
0.57	.....	.....	0.95	8.18	+ 0.36	2,980	4,525	44.77	.....
0.44	.....	.....	0.95	7.28	+ 1.32	2,375	3,980	43.82	0.177
0.38	.....	.....	0.95	7.56	+ 1.14	1,455	2,327	42.58	.....
0.52	.....	.....	0.95	7.90	+ 1.12	2,010	3,610	43.32	.....
0.35	.....	.....	1.34	7.90	+ 1.09	3,070	3,750	42.61	.....
0.55	.....	.....	1.34	8.62	+ 0.14	3,000	3,880	41.74	.....
0.49	.....	.....	1.34	8.40	+ 0.06	3,250	3,865	42.43	.....
0.68	.....	.....	1.34	9.07	+ 0.53	2,510	3,110	42.30	.....
0.75	.....	.....	1.34	8.51	+ 1.26	2,730	3.010	42.36	0.118
0.60	.....	.....	1.34	7.56	+ 2.18	2,850	3,650	42.55	.....
0.71	.....	.....	1.34	8.79	+ 2.15	2,800	3,030	41.79(?)	.....
....	.....	.....	....	....	....	2,605	1,565	42.67	.....

† Feces N calculated as 12% of Food N, up to November 26.

47 kg. After twenty-five days he was discharged weighing 57 kg. Glycosuria was said to have been 10 per cent. on admission, 5 per cent. on discharge. A dose of salts taken October 24 left him very weak, and thereafter he lost weight and strength rapidly. He was admitted to Rockefeller Hospital Nov. 7, 1914. Height 172 cm., weight 41.6 kg., extremely weak. Heart, lungs and abdomen negative; blood-pressure 85 systolic, 75 diastolic; clinical picture of acidosis, with drowsiness and increased respiration threatening coma. His diet containing

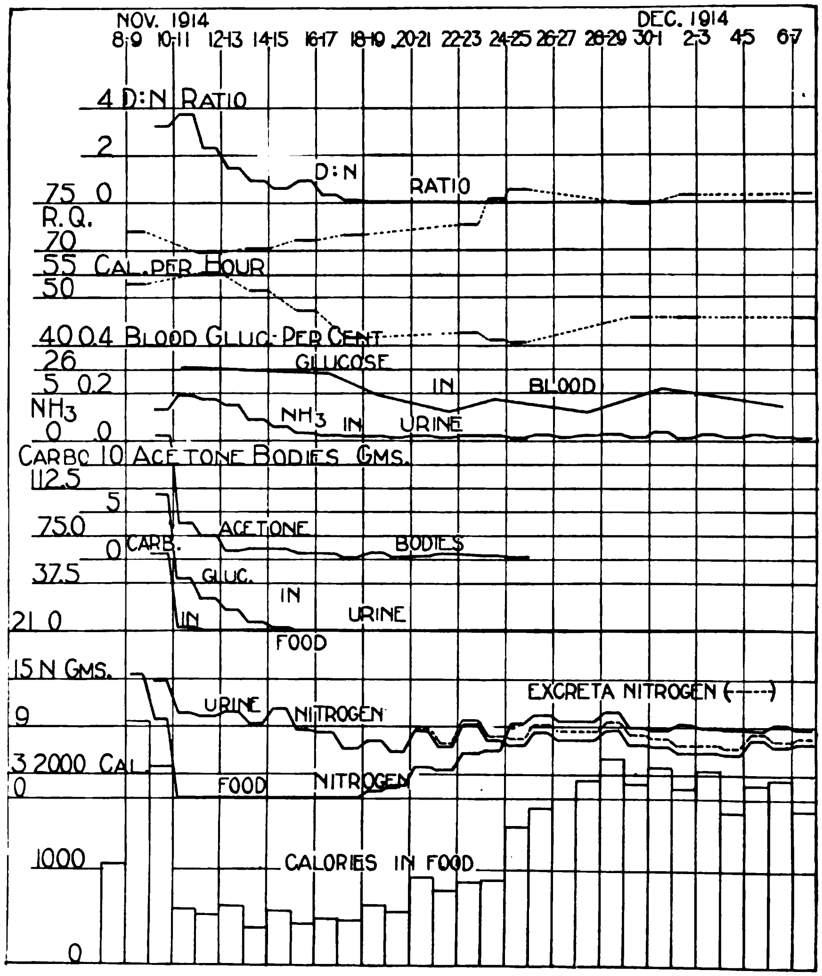

Fig. 2 (Gerald S.).—Laboratory findings shown graphically.

carbohydrate was continued, and he was transferred next day to the Russell Sage metabolism ward at Bellevue Hospital, where he remained until the close of the metabolism experiments, then returned to the Rockefeller Hospital.

The diet shown in Table 2 was all he could eat on November 8 to 10 inclusive. At 6 a. m. on November 11 he received 50 c.c. cream, then developed nausea without vomiting. Fasting was begun at this time because of the complete repugnance to food and the dangerously threatening coma symptoms. No bicarbonate was given except 10 gm. on November 11. The fast lasted eight days,

and the condition cleared up, as shown in the table. Alcohol was given in the form of whisky during the fast, in quantities just short of producing any discomfort or intoxication symptoms. Notwithstanding the extreme initial weakness, the clinical condition perceptibly improved during the fast. The first food added to the alcohol after the fast was protein—eggs at first, later meat. More protein and fat were gradually added, until the unduly high diet of over fifty calories per kilogram of weight was reached. Bulk was contributed to the diet by the use of from 750 to 1,000 gm. of thrice-boiled vegetables daily, some samples of which were analyzed for carbohydrate. The rapid gain in weight shortly after the fast was due to the water retention common in such patients. Improvement continued in subsequent treatment. The carbohydrate tolerance remained low, but the patient became able to exercise freely, and he and his parents considered him fit for work. For this reason he refused to be further controlled, and was dismissed from the hospital and from all further supervision, with due warning of the consequences. The discharge was on Feb. 8, 1915, the diet at that time being about 1,400 calories, with no glycosuria or ketonuria, and the body weight 44 kg. He progressed rapidly downward and died March 9, 1915.

Case 2.—William G. (severe diabetes), printer, age 29, married. Family, personal history and habits negative. Figure thin; normal weight from 66 to 69 kg. Thirst and dry mouth noticed in June, 1913. Progress was steadily downward in spite of treatment. Entered Presbyterian Hospital July 25, 1914. His condition there was dangerous on carbohydrate-free diet and worse when it was attempted to add carbohydrate. The dextrose-nitrogen ratio was found to be about 3. He was transferred to Rockefeller Hospital on July 28. Height 179 cm., weight 50 kg. Physical examination negative. Table 3 contains part of the laboratory data for this period. Carbodydrate of food was determined only by calculation. Other food values for the first two days are calculated. After that, nitrogen and fat were analyzed in food and feces.

Thus the emaciated patient, spending most of the twenty-four hours in bed and the rest of each day sitting limply in a chair, was unable to maintain his body weight even on utilizable calories in excess of the needs of a normal person of equal weight. The excess of fat failed to prevent nitrogen loss. Yet high protein feeding is known to aggravate diabetes, even though temporary nitrogen equilibrium is attained. This is the old dilemma. As soon as the appetite partly failed, on August 1, the nitrogen deficit became large. Fasting had to be inaugurated on August 2 because of symptoms of beginning coma. Along with the fall in glycosuria, within two days the level of nitrogen excretion characteristic of advanced inanition was attained. Feeding with green vegetables was commenced August 7. Gradual increase of vegetables up to August 12 showed a carbohydrate tolerance of 38.5 gm. Other food was then given, and there seemed to be satisfactory improvement, with glycosuria and ketonuria absent as usual. The case then differed from others in that a gradual loss of tolerance manifested itself; diagnosis was impossible for several months, but the apparent explanation of the trouble was at length found in pulmonary tuberculosis. Vain attempts were made several times to increase strength by high feeding with disregard of glycosuria. In January, 1915, with no sign of tuberculosis, the patient spent some time in the Russell Sage metabolism ward for investigation before and after such a period of high diet

TABLE 3.—WILLIAM G.: CLINICAL DATA DURING FIRST PART OF STAY IN THE ROCKEFELLER HOSPITAL

Date	Body Weight, Kg.	Water Intake, c.c.	Urine						Nitrogen Balance*	Food					Sodium Bicarbonate, Gm.	Calcium Carbonate, Gm.
			Volume, c.c.	Acetone Bodies as Beta-oxybutyric Acid, Gm.	Ammonia Nitrogen, Gm.	Dextrose Gm.	Dextrose-Nitrogen Ratio	Total Nitrogen, Gm.		Nitrogen, Gm.	Carbohydrate, Gm.	Alcohol, Gm.	Calories			
													In Food	Available†		
July 29-30......	49.4	1,800	3,424	26.05	2.88	61.63	2.6	23.27	— 6.86	17.29	6.9	...	2860.7	2448.1	..	20
July 30-31......	47.4	2,540	2,570	20.51	2.16	64.99	3.3	17.48	— 0.66	17.70	11.5	...	2693.9	2297.6	20	20
July 31-Aug. 1	47.0	2,200	2,970	19.69	2.73	58.24	2.7	20.49	+ 0.39	21.78	7.7	30	3135.5	2762.6	20	20
August 1-2.....	47.4	2,810	3,165	33.62	3.48	60.46	2.4	24.36	—12.63	12.61	5.8	30	2730.9	2261.2	20	20
August 2-3.....	47.4	2,642	1,285	15.56	4.25	17.85	1.2	14.83	—15.71	.....	....	102	714.0	593.9	30	20
August 3-4.....	48.0	1,950	2,185	8.80	2.06	1.93	0.26	7.22	....	.....	....	97	682.5	592.9	40	20
August 4-5.....	48.4	1,870	1,840	2.47	0.44	2.04	0.34	5.99	....	.....	....	80	560.0	499.3	10	5
August 5-6.....	48.2	2,092	2,815	2.09	0.88	0	....	7.04	....	.....	....	102	714.0	656.0	..	..
August 6-7.....	47.6	2,722	2,100	2.97	1.07	0	....	10.20	....	.....	....	92	644.0	582.2	..	..
August 7-8.....	47.0	2,785	2,365	4.95	1.16	0	....	6.72	— 7.26	0.34	5.8	82	610.3	535.0	..	..
August 8-9.....	47.2	2,545	1,625	3.10	1.06	0	....	7.66	— 7.69	0.85	15.7	85	688.6	626.2	..	..

* Average daily N in feces 0.876 gm.
† Calories lost in urine and feces subtracted from calories of diet.

(Table 4). He was subjectively and objectively so much better when kept free from glycosuria and ketonuria, that this was done nearly constantly until March 11, 1915. Then the course of the tuberculosis was beçoming very rapid. Death occurred from diabetes and bronchopneumonic tuberculosis on March 22, 1915.

CASE 3.—Joseph U. (severe diabetes), manufacturer, aged 44, married. His family, personal history and habits were negative. Normal weight 75 kg. In 1907, loss of weight, and medical diagnosis of diabetes. At first kept free from glycosuria occasionally by treatment, but it has been continuous for the past three or four years. Emaciation and weakness have been the principal symptoms. Patient was bedridden for the six weeks preceding admission to hospital. He was brought on a cot from his home in Indiana and entered Rockefeller Hospital Nov. 28, 1914. Height 179 cm., weight 44.2 kg. Physical examination was negative, except for emaciation and a yellow tinge like pernicious anemia, which diagnosis was excluded by blood examination. Blood pressure not certain. On January 18, when he appeared much stronger and was beginning to sit up a little, systolic blood pressure was 76, diastolic 60. Glycosuria and ketonuria heavy. Ammonia nitrogen 2.5 gm on November 28-29, 2.78 gm. on November 29-30. No symptoms of acidosis.

Treatment was conducted by Dr. Stillman. The patient fasted November 30 to December 7, inclusive, receiving 70 c.c. whisky daily, and on December 7 receiving also 500 gm. thrice-boiled vegetables. Eggs and butter were added gradually until on December 10 the diet contained 52 gm. protein, 95 gm. fat, 100 c.c. whisky, and 500 gm. thrice-boiled vegetables. On this day a glycosuria of 9.5 gm. appeared. The strength and well-being had improved from the outset; but though ketonuria had diminished, it had never cleared up satisfactorily. The carbohydrate tolerance was literally nothing. Details will be published elsewhere. Briefly, it was necessary to keep him on a diet of about 700 calories daily, about half of which was alcohol, until February 3. He was warm and quiet in bed except for short daily periods. The weight on February 3 was 40.3 kg., and strength continued to improve. It was toward the close of this prolonged undernutrition that the calorimeter tests were made, on January 31 and February 1. It then became possible to increase the diet somewhat, but fast-days were still used frequently. The ferric chlorid reaction slowly diminished to traces, but did not become regularly negative until the latter part of May. The patient was discharged June 28, 1915, at precisely his initial weight, namely, 44.2 kg., with urine normal on a diet of 80 gm. protein, 15 gm. carbohydrate and 1,950 calories. He has since conducted his business. Carelessness with his diet brought back glycosuria and required his return to the hospital on Oct. 17, 1915; but the condition was much more favorable than before and the tolerance higher on discharge from the hospital this time (Jan. 18, 1916) than on the previous occasion.

CASE 4.—Edward M. (moderately severe diabetes), customs inspector, aged 34, married. His family, personal history and habits were negative, except for chronic indigestion and constipation since the age of 22. Normal weight 80 kg. In July, 1913, occurred sudden attack of dizziness, colic, vomiting and diarrhea, with fever for one day. From that time on he was constantly thirsty and lost weight and strength. Diabetes diagnosed in September. Under inefficient treatment he was sugar-free for only two periods of one week each. Entered Rockefeller Hospital July 15, 1914. Weight 60.4 kg. Highly neurasthenic, but no serious emaciation or acidosis. Physical examination negative except for sallow color and enlarged liver. On restricted diet there was marked ketonuria and a negative carbohydrate balance of about 12 gm. Four days of fasting from July 18 to 21, inclusive, were required to stop glycosuria. Feeding was begun on July 23, with vegetables containing 12.2 gm. carbohydrate.

TABLE 4.—WILLIAM G.: CLINICAL DATA DURING STAY AT BELLEVUE HOSPITAL JANUARY 10 TO 15

Date	Body Weight, Kg.	Water Intake, c.c.	Urine						Nitrogen Balance	Food			
			Volume, c.c.	Diacetic Acid	Ammonia Nitrogen, Gm.	Dextrose, Gm.	Dextrose-Nitrogen Ratio	Total Nitrogen, Gm.		Nitrogen, Gm.	Carbo-hydrate, Gm.	Alcohol, Gm.	Calories
Jan. 10-11	43.3	2,130	1,465	....	1.48	0	....	5.27†	—0.17	5.8	...	57.4	1,775
Jan. 11-12	43.2	1,910	1,177	++	1.60	0	....	6.47	+1.14	9.78	0.6	30.6	2.016
Jan. 12-13	43.3	2,650	1,905	++	2.81	11.4	1.27	8.49	+1.13	10.03	0.6	57.4	2,441
Jan. 13-14	....	2,350	2,520	++	2.76	15.3	2.02	7.18	+1.99	10.42	0.6	57.4	2,250
Jan. 14-15	44.9	3,100	3,665	++	4.05	23.0	2.28	9.63	+1.73	12.91	1.0	57.4	2,738
Jan. 15-16*	44.0	1,150	876	....	1.18	9.9	3.98	2.42	......	4.41	0.4	11.5	902
Jan. 16-17	42.8	1,150	2,500	++	....	43.8	3.14	13.91	—3.96	11.3	...	20.0	1,811
Jan. 17-18	42.0	1,335	2,770	++	3.40	42.8	3.10	13.82	—3.19	12.06	...	20.0	2,305
Jan. 18-19	40.8	750	2,775	++	....	46.7	3.44	13.50	—2.96	12.06	...	22.5	2,183
Jan. 19-20	40.6	1,850	2,925	++	....	69.6	....	.....	......	14.3	2.2	20.0	2,369
Jan. 20-21	....	2,700	4,385	++	....	76.7	3.82	20.1	—6.51	14.29	...	20.0	2,335
Jan. 21-22	42.4	4,060	4,700	++	....	45.	....	.....	......	15.15	2.2	22.5	2,506
Jan. 22*	43	2,000	1,300	++	....	8.8	3.15	2.81	—2.81	.....	...	40.0	280

* Incomplete. † Only for the calorimeter periods.

TABLE 5.—Felix K.: Clinical Data

Date	Total Calories	Fat, Gm.	Carbo., Gm. in Food	Glucose, Gm. in Urine	N in Food, Gm.	N in Urine, Gm.	Body Weight, Kg.	Urine Volume, c.c.	Remarks
1/14/14	2,046	155.4	57.7	12.05	14.2	12.18	.....	820	
1/15/14	2,016	145.4	62.5	21.50	15.8	18.61	.....	1,000	
1/16/14	2,092	168.0	62.4	12.50	12.5	12.61	.....	920	
1/17/14	1,989	141.6	64.8	18.80	15.6	14.79	56.51	1,180	
1/18/14	2,304	177.7	58.2	10.00	16.0	15.19	.....	1,300	
1/19/14	2,065	149.0	64.8	6.45	16.9	11.99	56.88	940	
1/20/14	1,964	140.1	62.9	0	15.6	15.52	.....	1,580	
1/21/14	2,369	181.8	59.8	9.65	16.5	16.08	57.52	1,380	
1/22/14	2,667	216.4	60.4	9.11	15.8	12.16	56.52	1,170	
1/23/14	2,852	236.5	59.8	5.88	15.9	13.90	.....	1,360	
1/24/14	2,684	218.5	59.8	8.08	15.9	12.39	57.07	1,300	
1/25/14	3,188	247.4	59.8	5.68	16.0	10.31	.....	1,040	
1/26/14	2,788	178.7	59.8	7.14	16.1	11.77	56.76	1,360	
1/27/14	2,773	178.8	60.0	8.70	15.9	10.54	.....	1,200	
1/28/14	3,059	188.8	59.8	5.88	16.0	12.83	57.01	1,120	
1/29/14	921	76.7	20.8	0	4.7	9.36	.....	1,330	
1/30/14	2,986	179.9	60.5	0	16.2	13.84	56.98	1,460	
1/31/14	3,458	180.0	59.7	0	16.1	13.28	.....	1,520	
2/ 1/14	3,492	182.1	61.9	Trace	16.5	13.84	.....	1,600	
2/ 2/14	3,488	182.8	60.5	0	16.2	14.01	57.97	1,910	
2/ 3/14	3,492	208.8	60.5	6.88	16.2	12.95	.....	2,220	
2/ 4/14	3,579	192.2	60.5	8.08	16.5	11.77	58.76	1,860	
2/ 5/14	3,580	192.2	60.7	5.68	16.3	11.54	.....	1,640	
2/ 6/14	3,615	197.8	60.5	0	15.9	10.65	.....	1,400	
2/ 7/14	3,663	201.5	59.7	6.90	16.4	13.34	58.25	1,330	
2/ 8/14	3,620	186.8	60.5	10.00	16.3	11.21	.....	1,140	
2/ 9/14	3,310	181.6	62.3	8.34	16.2	13.17	.....	1,180	
2/10/14	982	81.7	20.8	0	5.3	9.92	58.17	1,300	Green day
2/11/14	929	77.1	20.8	0	5.1	9.33	57.56	1,155	Green day
2/12/14	2,188	124.1	178.1	18.80	9.9	11.59	57.84	1,515	Oatmeal day
2/13/14	2,177	127.1	178.1	19.22	10.3	10.87	57.98	1,580	Oatmeal day
2/14/14	2,171	126.7	178.1	31.08	10.2	10.54	57.80	1,930	Oatmeal day
2/15/14	917	76.1	20.8	0	4.8	9.92	.....	970	Green day
2/16/14	3,487	181.9	61.6	0	16.2	14.96	57.85	1,180	Green day
2/17/14	3,464	180.1	60.7	Trace	16.8	12.89	57.75	1,000	
2/18/14	3,421	175.9	60.1	13.20	16.1	14.74	58.88	1,650	
2/19/14	3,361	170.2	59.7	9.10	15.9	14.01	58.45	1,820	
2/20/14	3,469	181.1	59.7	13.70	16.1	16.08	58.24	1,600	

TABLE 5.—Felix K.: Clinical Data—(*Continued*)

Date	Total Calories	Fat, Gm.	Carbo., Gm. in Food	Glucose, Gm. in Urine	N in Food, Gm.	N in Urine, Gm.	Body Weight, Kg.	Urine Volume, c.c.	Remarks
2/21/14	3,347	171.2	59.5	5.88	15.0	11.10	58.89	1,810	
2/22/14	3,396	173.9	61.2	Traces	15.7	10.70	.....	1,460	
2/23/14	3,329	176.7	60.4	Traces	16.0	11.54	59.02	1,760	
2/24/14	3,318	174.8	38.6	Traces	14.7	11.45	59.17	1,405	Bread every two hours
2/25/14	3,460	181.3	58.8	Traces	16.0	12.10	.....	1,080	
2/26/14	920	76.6	20.6	0	4.8	9.09	58.60	1,110	
2/27/14	3,622	174.8	12.1	0	14.6	15.08	.....	1,480	
2/28/14	3,254	181.8	18.4	0	15.9	12.78	59.00	1,300	
3/ 1/14	3,494	218.4	38.2	0	14.4	15.08	.....	1,900	
3/ 2/14	3,341	177.6	39.6	0	15.6	15.60	59.16	2,120	
3/ 3/14	3,336	177.7	38.4	0	15.6	13.79	58.87	1,540	
3/ 4/14	3,375	177.6	47.2	0	15.8	12.72	59.51	1,400	
3/ 5/14	3,400	178.4	50.3	0	16.0	12.89	60.08	1,540	
3/ 6/14	3,486	179.6	65.0	0	16.5	12.69	60.07	1,440	
3/13/14	3,360	178.5	58.5	5.75	15.2	15.20	59.52	1,650	Oatmeal every two hours
3/14/14	943	78.4	20.8	0	5.0	10.87	59.37	1,400	Green day
3/15/14	927	77.1	20.8	0	4.8	5.77	59.22	870	Green day
3/16/14	2,007	112.0	178.0	24.39	9.1	10.31	.....	1,580	Bread day
3/17/14	2,013	112.6	178.0	27.03	9.2	8.85	58.81	1,390	Bread day
3/18/14	2,057	116.0	178.0	37.38	9.6	8.34	.....	1,786	Bread day
3/19/14	942	78.1	20.8	0	5.0	6.43	58.42	930	Green day
3/20/14	946	78.7	21.2	0	4.8	7.88	.....	1,377	Green day
3/21/14	3,388	173.1	61.4	0	15.6	11.93	.....	2,130	
3/22/14	3,359	173.4	58.3	15.86	14.9	10.31	.....	1,250	
3/23/14	3,164	199.5	66.7	Trace	15.0	11.04	.....	1,320	

The vegetables were increased until on July 30 he was taking 70.5 gm. carbohydrate, without glycosuria. Protein and fat were then slowly added, and an adequate diet attained without difficulty. Patient is a gourmand, and in September he was allowed to bring back his old symptoms by excess of fat in the diet, as an object-lesson. Two days' fasting stopped this glycosuria and suitable diet was resumed. In the latter part of October the average daily diet was approximately 114 gm. protein, 120 gm. carbohydrate, and from 2,600 to 2,900 calories. Calorimeter experiments were performed on October 30 and 31 and November 5. Patient was discharged on Nov. 9, 1915, weighing 61.2 kg. He has done his usual work since, with only an occasional temporary glycosuria after eating too much.

Case 5.—Felix K. (mild diabetes), clerk, 47 years old, born in Ireland. As a young man the patient had pneumonia, urethritis, and about four years ago an attack of malaria. He was a heavy drinker of beer and whisky up to five months ago. Lately he has taken but little alcohol. About one year ago he first noticed a loss of weight, with polyuria and weakness. Since then he has lost from 40 to 50 pounds. On admission to Bellevue, Oct. 28, 1913, he

was so weak that he could hardly walk upstairs. He is an emaciated man of medium stature. The lungs are emphysematous. There is slight exophthalmos, but no enlargement of the thyroid gland. Wassermann reaction + +; hemoglobin 98 per cent.; leukocytes 9,500; blood pressure: systolic 110, diastolic 75. His urine contained 61 gm. of glucose, 2.14 gm. ammonia, and small amounts of betaoxybutyric acid. The patient was in the general ward and it was difficult to control his diet. He was discharged on November 25, and on January 13 was readmitted, this time to the metabolism ward. Weight January 16, 56.5 kg. On a restricted diet his carbohydrate tolerance improved and his weight and strength increased rapidly (see Table 5). He was discharged March 24, 1914, in excellent condition. Since then he has reported from time to time, feeling perfectly well and strong, but showing sugar in the urine when he departs from his diet.

Case 6.—John O'C. (mild diabetes, morphinism), clerk, aged 32. His father was an alcoholic. At the age of 15 the patient had typhoid, and he has suffered from "pleurisy" eight times in the past few years. At the age of 16 he began to smoke opium, later taking to hypodermic injections of the drug, and one year ago he added cocain in increasing doses. Before admission he was taking 80 grains of cocain and 22 of morphin a day. This is his first attempt at breaking the habit. About two years ago he noticed polyuria and polydipsia and his doctor found sugar in the urine. He did not follow treatment and lost weight rapidly. He was very constipated, and so weak that he could hardly walk. Admitted to Bellevue Hospital March 13, weight March 24, 31.3 kg., height 163 cm. He was found to be nothing but skin and bones, toothless, with bent figure and ratlike, pathetic face. His whole body was covered with abscesses and scars of infections from hypodermic injections. There was a small ulcer on the sole of each foot. His pulse was very small, the beat normal, his tongue fissured, glassy and moderately red.

On a restricted diet the patient improved slowly and the glycosuria and acidosis cleared up (Table 6). He grew stronger but it was almost impossible to increase his weight without causing glycosuria. It was necessary to give him a grain of morphin every four hours. His systolic blood pressure varied between 104 and 125. On May 1, 1915, he was discharged and sent to a sanitarium, where he stayed a short time, then went back to his old habits and died a few months later.

SUMMARY AND COMMENT

1. *The Oatmeal Treatment.*—The mildly diabetic patient, Felix K., on a regulated diet containing about 60 gm. carbohydrate daily, showed a constantly positive carbohydrate balance and maintained his weight and well-being. February 10 and 11 were "green" days. Then from February 12 to 14, inclusive, 200 gm. oatmeal were given daily in the usual manner; then followed, Februry 15 to 16, two more "green" days. For comparison, beginning March 14, the same program was instituted, using bread instead of oatmeal, namely, first two "green" days, then March 16 to 18, inclusive, 265 gm. bread daily, equivalent in carbohydrate to the previous oatmeal, with fat, protein and calories also corresponding to the oatmeal period; then March 19 and 20 two more "green" days. Comparison was also made in a different manner, as follows: On February 24 he was given 18 gm. bread and 9 gm. butter every two hours, and on March 13 was given the equivalent carbohydrate in the form of 13.6 gm. oatmeal with 9 gm. butter every two hours.

TABLE 6.—John O'C.:

Date	Food					
	Total Calories	Protein, Gm.	Fat, Gm.	Carbo., Gm.	Alcohol, Gm.	Food, N, Gm.
March 24-25	2,333	66.1	184.2	85.7	.....	10.57
March 25-26	1,842	81.1	131.2	70.4	.....	12.97
March 26-27	2,095	69.0	160.9	77.0	.....	11.04
March 27-28	2,021	79.4	147.3	84.2	.....	12.70
March 28-29	2,410	82.1	185.9	83.9	.....	13.13
March 29-30	2,508	82.1	195.9	85.2	.....	13.13
March 30-31	2,610	106.6	186.6	87.3	11.47	17.06
March 31-April 1	2,279	87.5	164.3	56.6	22.94	14.00
April 1- 2	2,488	88.7	183.7	62.4	22.94	14.19
April 2- 3	1,999	69.6	137.8	43.2	22.94	11.13
April 3- 4	294	0	0	0	42.00	0
April 4- 5	1,378	35.7	90.6	16.6	45.90	5.71
April 5- 6	1,941	44.1	126.5	142.5	.....	7.05
April 6- 7	1,594	47.0	87.8	142.5	.....	7.52
April 7- 8	1,758	47.0	104.8	142.5	.....	7.52
April 8- 9	2,148	57.2	194.3	25.9	.....	9.15
April 9-10	1,489	39.8	132.0	23.9	.....	6.36
April 10-11	1,783	48.1	154.4	36.6	.....	7.70
April 11-12	2,282	71.3	193.2	47.1	.....	11.41
April 12-13	2,435	76.0	200.7	61.6	.....	12.16
April 13-14	2,321	77.9	199.2	36.5	.....	12.46
April 14-15	2,178	70.6	187.6	35.0	.....	11.29
April 15-16	1,728	28.9	145.6	28.5	39.10	4.62
Auril 16-17	1,784	43.7	144.8	23.8	22.94	4.62
April 17-18	1,600	34.4	114.4	25.3	42.00	5.50
April 18-19	1,748	31.0	128.5	25.5	45.90	4.96
April 19-20	1,579	41.4	110.2	41.5	30.59	8.62
April 20-21	1,919	49.6	152.8	32.8	22.94	7.93
April 21-22	1,854	49.2	148.0	28.2	22.94	7.87
April 22-23	1,962	77.3	140.3	41.4	22.94	12.37
April 23-24	2,063	100.9	142.2	40.8	22.94	16.14
April 24-25	1,679	67.6	115.2	41.8	22.94	10.82
April 25-26	385	16.8	34.0	.....	.....	2.69
April 26-27	1,761	99.0	133.0	23.9	.....	15.84
April 27-28	787	25.3	60.6	16.7	.....	4.05
April 28-29	1,652	47.5	93.4	143.6	.....	7.60
April 29-30	1,674	47.0	96.3	142.5	.....	7.52
April 30-May 1	1,652	47.5	93.4	143.6	.....	7.60

Clinical Data

Urine							Body Weight Kg.
Urine N, Gm.	Excreta N, Gm.§	N Balance, Gm.	Urine Glucose, Gm.	Urine NH₃, Gm.	Diacetic Acid	Urine Volume, c.c.	
13.34	14.40	—3.92	78.1	....	....	1,395	31.25
12.72	14.02	—1.05	55.7	1.70	Small amount	1,130	31.94
.....	.....	......	....	....	....	.....	32.16
{ 9.53* 9.98†	11.20	+1.50	39.4	....	....	900	32.61
10.09	11.40	+1.73	43.7	....	....	1.480	33.30
9.92	11.23	+1.90	70.9	2.04	++	2,310	33.38
9.25	10.95	+6.11	53.3	1.30	+	2,000	33.63
10.54	11.94	+2.06	40.6	2.18	+++	1,550	33.14
9.53	10.95	+3.24	33.4	1.96	++	1,125	32.89
9.25	10.36	+0.97	23.6	1.06	+	920	32.89
6.02	.....	......	+++	0.67	0	500	32.11
6.31	7.33	—1.67	0	0.26	0	735	32.69
8.41	9.12	—2.09	20.7	0.41	0	1,280	.....
6.44	7.19	+0.33	40.6	0.41	....	3,875	34.31
4.51	5.35	+2.17	29.7	0.75	0	2,900	32.71
5.76	6.68	+2.47	Heavy trace	0.57	0	1,490	32.26
6.72	7.36	—1.00	0	0.61	0	2,670	32.52
7.31	8.09	—0.39	0	0.39	....	1,620	31.79
6.22	7.36	+4.05	0	0.49	0	1,400	.....
8.28	9.50	+2.66	11.8	0.96	0	2,570	32.38
6.73	7.98	+4.48	7.2	0.82	Slight trace	1,440	31.79
8.99	10.12	+1.17	11.4	1.12	+	2,240	32.46
5.55	6.01	—1.39	2.6	0.79	Trace	1,200	32.52
5.04	5.74	+1.25	Slight trace	0.76	Heavy trace	1,380	32.12
5.04	5.59	—0.09	....	....	....	2,500	.....
5.37	5.87	—0.91	....	....	....	1,925	32.05
6.22	7.08	+1.54	0	....	0	1,820	31.61
5.80	6.59	+1.34	....	....	....	1,840	32.35
5.39	6.18	+1.69	0	0.51	0	1,940	32.52
6.35	7.59	+4.78	0	0.47	0	2,000	32.25
9.83	11.44	+4.70	0	0.59	0	1,725	32.45
9.18	10.26	+0.56	4.8	....	0	825	32.44
6.37	6.64	—3.95	0	....	Very heavy trace	600	.....
11.43	13.01	+2.79	0	0.98	Heavy trace	960	31.04
9.30	9.71	—5.66	0	0.93	Slight trace	660	31.38
8.58	9.34	—1.74	15.9	1.04	Trace	1,105	31.43
6.43	7.23	+0.29	21.2	1.14	0	1,960	32.46
6.39	7.15	+0.45	23.1	1.17	0	1,825	32.45

* 23 hours. † 24 hours. § Urine N + 10 per cent. of Food N.

Subject, Date, Weight, Surface Area Linear Formula	Period	End of Period	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.
Gerald S.	Prelim.	11:15	.....	.....	.....	.....	.....	.....	.....
11/9/14 42.15 Kg. 1.44 Sq. M.	1	12:15	15.94	16.17	0.717	20.22	0.561	52.19	43.97
	2	1:15	16.32	16.39	0.724	20.85	0.561	52.94	47.51
	3	2:15	16.34	16.58	0.717	20.96	0.561	53.55	51.11
Gerald S.§.........	Prelim.	11:15	.....	.....	.....	.....	.....	.....	.....
11/12/14 40.15 Kg. 1.41 Sq. M.	1	12:15	16.27	15.87	0.746§	22.44	0.307	52.15	49.24
	2	1:15	16.95	17.45	0.706	23.81	0.307	56.71	54.44
	3	2:15	15.50	17.61	0.640	24.32	0.307	57.19	56.77
Gerald S.	Prelim.	10:24	.....	.....	.....	.....	.....	.....	.....
11/14/14 38.97 Kg. 1.40 Sq. M.	1	11:24	15.41	16.00	0.700	17.66	0.441	51.87	45.12
	2	12:24	15.85	15.84	0.705	18.65	0.441	51.35	49.55
	3	1:24	15.30	15.87	0.701	18.71	0.441	51.45	51.61
Gerald S.	Prelim.	11:22	.....	.....	.....	.....	.....	.....	.....
11/16/14 38.77 Kg. 1.40 Sq. M.	1	12:22	13.85	14.29	0.705	29.82	0.347	46.34	43.67
	2	1:22	14.59	14.84	0.715	26.65	0.347	48.18	49.69
	3	2:22	15.27	14.73	0.754	24.96	0.347	48.25	50.03
	4	3:22	14.53	15.57	0.680	23.60	0.347	50.55	49.39
Gerald S.	Prelim.	11:06	.....	.....	.....	.....	.....	.....	.....
11/18/14 38.74 Kg. 1.40 Sq. M.	1	12:06	12.17	12.41	0.713	13.42	0.247	40.40	34.51
	2	1:06	13.00	13.45	0.718	13.97	0.247	42.82	38.89
	3	2:06	14.19	13.43	0.769	14.61	0.247	44.27	41.69
	4	3:06	13.76	14.44	0.693	14.75	0.247	47.06	44.15
	5	4.06	13.45	13.06	0.685	14.47	0.247	42.85	40.50
Gerald S.	Prelim.	11:06	.....	.....	.....	.....	.....	.....	.....
11/20/14 38.74 Kg. 1.40 Sq. M.	1	12:06	13.37	12.50	0.778	17.60	0.22	41.60	39.42
	2	1:06	12.20	12.82	0.692	16.68	0.22	42.06	41.23
	3	2:06	12.28	12.13	0.736	16.19	0.22	39.92	41.02
	4	3:06	15.43	14.29	0.785	16.43	0.22	47.67	43.08
Gerald S.	Prelim.	11:15	.....	.....	.....	.....	.....	.....	.....
11/23/14 42.84 Kg. 1.45 Sq. M.	1	12:15	13.02	13.54	0.699	12.99	0.232	44.14	38.70
	2	1:15	13.64	12.61	0.786	13.10	0.232	41.76	38.23
	3	2:15	12.56	13.11	0.697	14.15	0.232	42.72	42.79
Gerald S.	Prelim.	11:06	.....	.....	.....	.....	.....	.....	.....
11/24/14 44.00 Kg. 1.46 Sq. M.	1	12:06	12.80	11.70	0.796	13.09	0.237	38.79	36.04
	2	1:06	13.56	13.94	0.707	13.95	0.237	45.44	39.79
	3	2:06	13.22	12.51	0.768	13.69	0.237	41.23	38.55
	4	3:06	12.10	11.85	0.742	14.13	0.237	38.78	38.96

§ Calculations in summary based on total O_2 and CO_2 for 3 hours.

Direct Calorimetry (Rectal Temp.), Cal.	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M. Mech	
.....	36.28	..	....	.....	....	....	....	....	.....	Basal; D:N assumed to be 1.53 on basis of R.Q. Very quiet
55.18	36.61	71	4	0.704	22.4	77.6	0	1.24	35.01	
55.57	36.85	76	8	0.714	22.1	77.9	0	1.26	35.51	
51.18	36.86	77	4	0.705	21.8	78.2	0	1.27	35.92	
.....	37.14	..	....	.....	....	....	....	....	.....	Second day of fast; basal
52.23	37.24	99	7.2	0.755	8.0	75.1	16.9	1.30	36.11	Asleep 50 min.
54.77	37.26	102	10.5	0.711	7.4	91.3	1.3	1.41	39.27	Asleep 40 min.
55.45	37.23	99	2.0	0.639*	7.3	92.7	0	1.42	39.61	Asleep 30 min.
.....	36.54	..	....	.....	....	....	....	....	.....	Fourth day of fast; basal
49.33	36.68	81	7.8	0.68*	19.4	80.6	0	1.33	36.66	Asleep
41.18	36.42	..	7.6	0.69*	19.6	80.4	0	1.32	36.29	Asleep
51.95	36.44	79	12.0	0.68*	19.5	80.5	0	1.32	36.36	Asleep 45 min.
.....	36.16	..	....	.....	....	....	....	....	.....	Basal
40.14	36.08	..	9.0—	0.695	15.5	84.5	0	1.20	32.86	Asleep
53.54	36.16	..	13.0—	0.708	14.8	84.0	1.2	1.24	34.17	Asleep
48.88	36.06	70	15.8—	0.754	14.8	72.4	12.8	1.25	34.22	Drank 20 c.c. whisky at 1:27 p. m.
49.10	36.08	..	17.0—	0.665	14.2	85.8	0	1.30	35.85	Asleep
.....	35.76	..	....	.....	....	....	....	....	.....	Basal
26.05	35.51	..	4	0.697	15.5	84.5	0	1.04	28.65	Asleep
39.33	35.52	..	4	0.705	14.6	85.4	0	1.11	30.37	Basal, asleep
53.62	35.84	..	12	0.764	14.1	70.1	15.8	1.14	31.40	Drank 20 c.c. whisky at 1:06 p. m. Asleep 40 min.
53.62	36.14	..	13	0.676	13.2	86.8	0	1.22	33.38	Asleep 55 min.
34.91	35.97	..	7	0.740	14.6	75.5	9.9	1.11	30.39	Asleep 55 min.
.....	35.88	..	....	.....	....	....	....	....	.....	Whisky, 20 c.c. at 11:06 a. m.
37.70	35.78	..	6	0.773	14.7	66.7	18.6	1.07	29.50	Dozed
40.06	35.75	..	4	0.673	14.5	85.5	0	1.09	29.83	Dozed
42.74	35.81	..	3	0.724	15.3	79.2	5.5	1.03	28.31	Dozed
46.44	35.92	..	19	0.782	12.8	65.2	22.0	1.23	33.04	Restless
.....	35.99	..	....	.....	....	....	....	....	.....	Basal
37.09	35.95	47	8	0.681	13.9	86.1	0	1.03	29.29	Asleep 30 min.
43.05	36.04	..	11	0.788	14.7	63.8	21.5	1.00	27.71	Awake
34.37	35.81	52	14	0.678	14.4	85.6	0	1.00	28.35	Awake
.....	35.85	..	....	.....	....	....	....	....	.....	Basal
36.30	35.85	52	4.0	0.794	16.2	59.9	23.9	0.90	25.29	Quiet
41.16	35.90	51	5.5	0.691	13.8	86.2	0	1.08	29.62	Quiet
40.63	35.96	..	5.0	0.762	15.2	69.2	15.6	0.94	26.88	Drank 1 drop of water
31.21	35.75	50	2.2	0.730	16.2	76.9	6.9	0.90	25.28	Quiet

* R. Q. assumed as 0.707 for calculations.

Subject, Date, Weight, Surface Area Linear Formula	Period	End of Period	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calo-rimetry, Cal.	Heat Elimi-nated, Cal.
Gerald S. .... 11/25/14 44.04 Kg. 1.46 Sq. M.	Prelim.	11:15	.....	.....	.....	.....	.....	.....	.....
	1	12:15	12.72	12.29	0.753	14.98	0.235	40.82	36.55
	2	1:15	13.21	12.40	0.775	15.14	0.235	40.96	37.95
	3	2:15	13.08	12.29	0.771	15.61	0.235	40.59	38.83
	4	3:15	11.87	12.68	0.680	15.97	0.235	41.81	40.58
Gerald S. .... 11/30/14 44.27 Kg. 1.47 Sq. M.	Prelim.	11:27	.....	.....	.....	.....	.....	.....	.....
	1	12:27	14.33	14.09	0.742	21.28	0.228	46.18	39.28
	2	1:27	14.07	13.45	0.760	20.78	0.228	44.27	42.66
	3	2:27	14.80	14.13	0.762	20.24	0.228	46.63	41.57
	4	3:27	14.36	14.27	0.732	20.30	0.228	46.67	45.91
Gerald S. .... 12/2/14 44.76 Kg. 1.47 Sq. M.	Prelim.	11:12	.....	.....	.....	.....	.....	.....	.....
	1	12:12	15.59	15.21	0.745	24.90	0.208	50.08	42.79
	2	1:12	13.27	12.57	0.768	22.51	0.208	41.48	42.54
	3	2:12	16.92	16.38	0.751	24.10	0.208	54.02	50.44
	4	3:12	14.97	13.99	0.779	23.89	0.208	46.31	44.84
Gerald S. .... 12/4/14 43.94 Kg. 1.46 Sq. M.	Prelim.	11:09	.....	.....	.....	.....	.....	.....	.....
	1	12:09	15.81	14.79	0.778	19.79	0.204	48.99	41.33
	2	1:09	16.48	.....	.....	19.61	0.204	50.91*	44.13
	3	2:09	13.93	13.34	0.759	18.19	0.204	43.95	42.59
	4	3:09	14.85	14.58	0.743	18.78	0.204	47.68	45.98
Gerald S. .... 12/7/14 42.58 Kg. 1.45 Sq. M.	Prelim.	11:10	.....	.....	.....	.....	.....	.....	.....
	1	12:10	14.77	13.78	0.780	18.90	0.216	45.69	40.83
	2	1:10	15.08	15.19	0.722	19.31	0.216	49.59	45.09
	3	2:10	13.93	13.15	0.770	18.21	0.216	43.48	44.85
	4	3:10	14.40	13.69	0.765	18.41	0.216	45.18	45.10
William G. .... 1/11/15 43.28 Kg 1.53 Sq. M.	Prelim.	11:20	.....	.....	.....	.....	.....	.....	.....
	1	12:20	13.39	12.62	0.772	16.14	0.170	41.83	40.94
	2	1:20	14.30	13.84	0.750	16.38	0.170	45.67	43.05
	3	2:20	13.74	14.26	0 .701	16.45	0.170	46.60	47.13
William G. .... 1/15/15 43.84 Kg. 1.54 Sq. M.	Prelim.	11:07	.....	.....	.....	.....	.....	.....	.....
	1	12:07	15.11	14.72	0.747	24.83	0.291	48.34	42.16
	2	1:07	14.49	15.73	0.670	24.11	0.291	51.03	47.43
	3	2:07	14.21	14.66	0.705	24.30	0.291	47.56	49.04
William G. .... 1/22/15 37.87 Kg. 1.46 Sq. M.	Prelim.	11:12	.....	.....	.....	.....	.....	.....	.....
	1	12:12	15.29	16.38	0.679	17.02	0.332	53.05	49.13
	2	1:12	14.80	15.66	0.688	17.32	0.332	50.69	48.96
	3	2:12	15.46	15.87	0.708	18.36	0.332	51.42	51.38

* Calc., from CO_2, R. Q. assumed 0.778.

—EXPERIMENTS—(*Continued*)

Direct Calorimetry (Rectal Temp.), Cal.	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M. Meeh	
.....	36.12	..	....	.....	....	....	....	....	.....	Basal
33.16	36.03	48	3.5	0.743	15.4	74.8	9.8	0.97	26.27	Dozed
37.01	36.01	..	2.7	0.769	15.2	66.3	18.5	0.98	26.68	Dozed
37.25	35.95	..	0.5	0.765	15.4	66.2	18.4	0.92	26.44	At 1:17 drank 20 c.c. whisky from tube
33.07	35.75	51	2.8	0.659	15.1	84.9	0	0.94	26.91	Dozed
.....	36.31	..	....	.....	....	....	....	....	.....	Basal
37.96	36.28	58	4.7	0.782	13.1	79.8	7.1	0.86	24.61	Quiet
46.36	36.40	53	8.5	0.753	13.7	73.4	12.9	1.00	28.78	Quiet
40.21	36.32	56	16.5	0.755	13.0	71.0	16.0	1.05	30.26	Drank 170 c.c. water at 1:28 p. m.
44.22	36.28	52	9.4	0.720	13.0	82.8	4.2	1.05	30.29	Quiet
.....	36.66	..	....	.....	....	....	....	....	.....	Basal
39.51	36.58	56	5.1	0.788	11.1	78.6	10.3	1.12	32.24	Quiet
37.03	36.44	55	1.1	0.762	13.3	70.8	15.9	0.98	26.78	Quiet
52.36	36.50	58	15.4	0.745	10.2	76.3	13.5	1.21	34.81	Exercised 10 min.
49.81	36.64	53	5.8	0.774	11.9	68.9	19.2	1.04	29.84	Quiet
.....	36.08									
48.84	36.29	58	2.6	0.773	11.0	69.6	19.4	1.12	31.96	Exercised 10 min.
51.94	36.51	..	5.7	.....	....	....	....	....	.....	Exercised 10 min.
43.85	36.55	59	2.9	0.752	12.3	74.6	13.2	1.00	28.67	Quiet
43.22	36.48	..	2.8	0.784	11.3	81.4	7.3	1.09	31.11	Quiet
.....	36.46	..	....	.....	....	....	....	....	.....	Basal
43.09	36.53	55	21.2	0.776	12.5	65.4	22.0	1.07	30.42	Quiet
48.78	36.64	56	19.4	0.711	11.6	87.2	1.2	1.17	33.02	Quiet
43.58	36.61	54	25.4	0.765	13.2	67.9	18.9	1.02	28.96	Quiet
44.95	36.61	56	23.6	0.759	12.7	71.3	16.1	1.06	30.08	Quiet
.....	36.76	..	....	.....	....	....	....	....	.....	Basal
42.16	36.80	65?	2.9	0.767	10.8	69.7	19.5	0.97	27.57	Asleep
38,53	36.68	65?	10.7	0.743	9.8	79.7	10.5	1.10	30.10	Awake, quiet
48.46	36.72	58	7.4	0.689§	9.7	90.3	0	1.10	30.72	Awake, quiet
.....	36.75	..	....	.....	....	....	....	....	.....	Basal, D:N 3.81 †
37.58	36.63	64	7.0	0.757	7.9	75.2	16.9	1.10	31.57	Asleep
47.22	36.63	64	9.6	0.678	7.4	92.6	0	1.16	33.33	Asleep
52.84	36.74	62	9.6	0.712	8.0	90.7	1.3	1.10	31.06	Asleep
.....	36.98	..	....	.....	....	....	....	....	.....	Basal, D:N 3.12
46.18	36.89	64	8.5	0.679	10.8	89.2	0	1.40	33.19	Dozed
46.55	36.82	64	2.2	0.689	11.3	88.7	0	1.34	36.50	Quiet
52.30	36.84	63	6.5	0.713	11.1	88.9	0	1.40	37.02	Quiet

† D:N assumed as 3.65 for calculations.
§ R. Q. assumed as 0.707 for calculations.

TABLE 7.—Data of Calorimeter—

Subject, Date, Weight, Surface Area Linear Formula	Period	End of Period	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calo-rimetry, Cal.	Heat Elimi-nated, Cal.
Joseph U. .... 2/1/15 40.14 Kg. 1.45 Sq. M.	Prelim.	11:15	.....	.....	.....	.....	.....	.....	.....
	1	12:15	11.56	11.45	0.734	18.41	0.188	37.45	42.09
	2	1:15	11.57	11.26	0.747	17.79	0.188	36.90	42.18
	3	2:15	11.39	11.07	0.748	16.90	0.188	36.36	40.80
Edward M. .... 10/30/14 60.59 Kg.	Prelim.	11:15	.....	.....	.....	.....	.....	.....	.....
	1	12:15	20.58	18.19	0.823	25.35	0.391	60.77	62.97
	2	1:15	20.88	19.29	0.787	26.61	0.391	63.80	66.38
Edward M. .... 10/31/14 60.92 Kg.	Prelim.	11:33	.....	.....	.....	.....	.....	.....	.....
	1	12:33	21.62	19.88	0.791	23.02	.....	66.23	54.37
	2	1:33	21.04	20.01	0.765	23.56	.....	66.29	61.79
	3	2:33	22.64	20.27	0.812	24.87	.....	67.89	66.77
Edward M. .... 11/5/14 62.16 Kg.	Prelim.	11:17	.....	.....	.....	.....	.....	.....	.....
	1	12:17	24.93	23.98	0.756	28.04	0.594	78.49	67.80
	2	1:17	25.27	24.55	0.748	28.96	0.594	80.21	76.64
	3	2:17	24.33	23.40	0.756	28.88	0.594	76.57	79.61
Felix K. .... 2/11/14 57.56 Kg.	Prelim.	11:15	.....	.....	.....	.....	.....	.....	.....
	1	12:15	20.18	19.36	0.758	22.51	0.325	63.74	66.09
	2*	2:15	44.10	43.06	0.745	44.78	0.650	141.40	140.20
Felix K. .... 2/12/14 57.84 Kg.	Prelim.	12:05	.....	.....	.....	.....	.....	.....	.....
	1	1:05	25.25	24.14	0.761	25.89	0.607	79.14	71.51
	2	2:05	26.63	24.85	0.779	31.64	0.607	81.91	89.43
	3	3:05	24.91	23.94	0.757	41.94	0.607	78.40	96.59
Felix K. .... 2/14/14 57.80 Kg.	Prelim.	11:08	.....	.....	.....	.....	.....	.....	.....
	1	12:08	25.79	23.83	0.787	23.97	0.481	78.91	75.60
	2	1:08	24.78	21.55	0.836	26.91	0.481	72.18	78.93
	3	2:08	24.53	21.55	0.828	27.69	0.481	72.03	80.44
Felix K. .... 2/24/14 58.70 Kg.	Prelim.	12:20	.....	.....	.....	.....	.....	.....	.....
	1	1:20	22.67	21.44	0.769	18.70	0.362	70.96	78.23
	2	2:20	22.61	20.08	0.819	19.99	0.362	67.13	77.64
	3	3:20	22.89	21.19	0.786	20.82	9.362	70.27	76.74
Felix K. .... 2/26/14 58.57 Kg.	Prelim.	11:02	.....	.....	.....	.....	.....	.....	.....
	1	12:02	21.00	.....	.....	18.95	0.326	.....	75.40
	2	1:02	21.76	20.52	0.771	20.88	0.326	67.66	76.05
	3	2:02	21.64	19.60	0.803	20.55	0.326	65.30	74.30
Felix K. .... 3/18/14 59.29 Kg.	Prelim.	11:50	.....	.....	.....	.....	.....	.....	.....
	1	12:50	21.60	20.44	0.768	21.60	0.789	66.62	74.07
	2	1:50	21.63	20.81	0.774	20.94	0.789	66.29	72.80
	3	2:50	22.03	20.08	0.800	21.42	0.789	65.80	73.09

—Experiments—(*Continued*)

Direct Calorimetry (Rectal Temp.), Cal.	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M. Mesh	
.....	36.56	..	....	....	....	....	....	....	.....	Basal
36.33	36.89	72	3.0	0.723	13.3	82.6	4.1	0.93	25.95	Very quiet
40.52	36.85	72	2.5	0.738	13.5	76.5	10.0	0.92	25.63	Very quiet
30.62	36.05	78	12.0	0.739	13.7	76.3	10.0	0.91	25.20	Quiet
.....	37.31	..	....	....	....	....	....	....	.....	Basal
55.09	37.16	52	34	0.827	17.1	48.0	35.0	1.00	32.74	Restless
55.99	36.96	53	21	0.784	16.3	70.2	21.1	1.05	34.37	Quiet
.....	36.76	..	....	.....	....	....	....	....	.....	97 gm. olive oil at 10:03 a. m.
58.10	36.84	64	27	.....	....	....	....	1.09	34.74	Quiet
65.49	36.92	60	20	.....	....	....	....	1.09	34.78	Quiet
66.45	36.92	55	46	.....	....	....	....	1.11	35.62	Restless
.....	.....	..	....	.....	....	....	....	1.10	35.00	Urine lost
.....	36.94	..	....	.....	....	....	....	....	.....	Breakfast at 7; 96 gm. olive oil at 9:17 a. m.
69.54	36.98	71	....	0.743	20.0	70.7	9.3	1.26	40.63	Quiet
78.39	37.02	60	....	0.734	19.6	73.8	6.6	1.29	41.52	Quiet
73.80	37.01	67	....	0.743	20.6	70.2	9.2	1.23	39.63	Quiet
.....	37.18	..	....	.....	....	....	....	....	.....	Basal
49.49	36.84	..	5.6	0.751	14	73	13	1.11	34.74	Asleep
148.21	37.06	69	38.5	0.736	12	79	9	1.23	38.53	Fairly quiet
.....	37.53	..	....	.....	....	....	....	....	.....	At 10:45 to 10:52: oatmeal, 125; butter, 15; protein, 18.8; fat, 19.8; carb., 89.1
64.43	37.39	80	6.8	0.749	20	68	12	1.37	42.99	
89.21	37.42	79	24.4	0.773	20	62	18	1.42	44.49	
88.69	37.28	71	26.0	0.744	21	69	10	1.35	42.59	
.....	37.21	..	....	.....	....	....	....	....	.....	At 9:45 to 9:53: oatmeal, 125; butter, 15
70.91	37.12	76	12.5	0.783	16	62	22	1.37	42.89	
78.10	37.11	..	21.9	0.848	18	44	38	1.25	39.23	
80.50	37.17	85	13.0	0.833	18	47	35	1.25	39.15	
.....	37.19	..	....	.....	....	....	....	....	.....	Bread, 18; butter, 9, every 2 hrs., last taken at 11:37 a. m.
71.53	37.06	..	7.5	0.774	14	66	20	1.21	38.15	
74.35	37.00	69	8.3	0.822	14	52	34	1.14	36.09	
77.84	37.03	75	7.4	0.788	14	63	23	1.19	37.78	
.....	37.08	..	....	.....	....	....	....	....	.....	Basal
72.11	37.02	72	6.8	.....	....	....	....	....	.....	Very quiet
73.10	37.06	..	7.9	0.769	13	68	19	1.15	36.44	Very quiet
74.45	37.07	75	10.0	0.802	13	59	28	1.12	35.16	Very quiet
.....	36.87	..	....	.....	....	....	....	....	.....	Oatmeal 13.6, butter 9, every 2 hrs., last taken at 11:07 a. m.; asleep 1st period and half of second
65.35	36.70	76	9.0	0.751	31	58	11	1.12	35.59	
72.95	36.71	76	7.2	0.760	32	55	13	1.12	35.41	
74.71	36.75	75	13.2	0.798	32	47	21	1.11	35.15	

TABLE 7.—DATA OF CALORIMETER—

Subject, Date, Weight, Surface Area Linear Formula	Period	End of Period	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.
Felix K. 3/18/14	Prelim.	11:25	.....	.....	.....	.....	.....	.....	.....
58.38 Kg.	1	12:25	23.83	22.18	0.781	22.75	0.373	73.47	71.91
	2	1:25	24.44	21.90	0.812	25.72	0.373	73.12	79.87
	3	2:25	22.15	19.18	0.840	24.78	0.373	64.42	73.67
	4	3:25	22.07	19.81	0.810	24.28	0.373	66.04	74.31
Felix K. 3/20/14	Prelim.	12:00	.....	.....	.....	.....	.....	.....	.....
57.84 Kg.	1	1:00	18.79	17.54	0.779	18.15	0.338	57.97	60.50
	2	2:00	20.17	19.60	0.748	19.90	0.338	64.34	65.02
	3	3:00	20.25	18.92	0.778	20.94	0.338	62.58	64.95
John O'C. 4/28/15	Prelim.	11:34	.....	.....	.....	.....	.....	.....	.....
31.43 Kg. 1.20 Sq. M.	1	12:34	14.26	9.92	0.782	24.34	0.381	46.05	47.99
	2	1:34	15.07	9.45	0.812	24.86	0.381	44.74	48.82
John O'C. 4/30/15	Prelim.	11:46	.....	.....	.....	.....	.....	.....	.....
32.45 Kg. 1.22 Sq. M.	1	12:46	14.25	12.85	0.804	22.96	0.262	42.80	43.58
	2	1:46	14.87	14.14	0.765	26.25	0.262	46.63	50.53

Glycosuria: The urine always became promptly and completely sugar-free on "green" days. The total amount of glucose excreted during the oat period was 64.1 gm., during the bread period 88.8 gm. This difference is fully comparable to those in the literature upon which the claims of superiority of oatmeal have been based. But, as Blum pointed out, spontaneous fluctuations in diabetic glycosuria must be allowed for, even when all conditions are kept as uniform as possible, and a repetition of the same test sometimes gives a variation in the opposite direction. The more favorable carbohydrate balance in this instance speaks no more for oatmeal than the less favorable nitrogen balance during this same time speaks against oatmeal. This interpretation is supported by the results of the other test; for on the days when the carbohydrates were given in small divided doses it so happened that the glycosuria from bread was only a trace, while that from oatmeal amounted to 5.75 gm. A consistent difference in favor of oatmeal is therefore not present.

Respiration Experiments: This patient on February 12, while fasting in the morning after a "green" day of eggs, butter and green vegetables of the 5 per cent. class, derived from 10 to 13 per cent. of the calories from carbohydrate. On the first oatmeal day he derived 13

—Experiments—(*Continued*)

Direct Calorimetry (Rectal Temp.), Cal.	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M. Meeh	
.....	37.16	..	....	.....	....	....	....	....	.....	At 9:45 to 10:06 a.m., bread 168, butter 15
63.34	36.99	67	11.3	0.777	13	66	21	1.12	39.67	
81.41	37.07	73	28.8	0.813	14	55	31	1.25	39.48	
69.51	37.01	71	22.2	0.847	15	44	41	1.10	34.78	
68.62	36.94	70	27.0	0.811	15	55	30	1.18	35.66	
.....	36.88	..	....	.....	....	....	....	....	.....	Basal
51.32	36.65	59	10.6	0.774	15	65	20	1.00	31.51	Asleep 30 min.
66.74	36.80	60	15.1	0.739	14	76	10	1.11	34.97	Quiet
67.66	36.88	62	13.3	0.774	14	66	20	1.08	34.01	Quiet
.....	36.43	..	....	.....	....	....	....	....	.....	1st oatmeal day. Oatmeal 50, butter 10, at 6:30 a. m. and again at 9:34 a. m., restless 2d period
45.42	36.34	58?	16.1	0.711	21.9	77.0	1.1	1.47	37.56	
48.22	36.33	76?	22.8	0.814	22.6	50.0	27.4	1.42	36.49	
.....	36.32	..	....	.....	....	....	....	....	.....	3d oatmeal day. Same food as above
42.28	36.27	67	9.0	0.807	16.2	54.1	29.7	1.32	34.19	Quiet
46.71	36.15	72	18.0	0.757	14.9	69.4	15.7	1.44	37.25	Restless

per cent., and on the third oatmeal day 32 per cent. from carbohydrate. If the metabolism of carbohydrate continued at this rate of 32 per cent. throughout the day, he could have utilized about 145 gm. The positive carbohydrate balance on that day was 149 gm. On March 18, the third day on which he received the same amount of starch in the form of bread, he derived 31 per cent. of his calories from this source; he utilized about 130 gm., and the positive balance was 147 gm. He was able to derive 26 per cent. of his calories from carbohydrate after small divided meals of bread and butter, and as much as 24 per cent. while fasting on the morning after his usual diet, which just kept him sugar-free. After similar doses of oatmeal he derived only 15 per cent. from carbohydrate. The respiration experiments therefore show no significant difference between the starch of bread and that of oatmeal in this case.

The morphin addict, John O'C., with mild diabetes, gave exactly the same results, namely, on the first oatmeal day, April 28, 14 per cent. from carbohydrate, on the third day, April 30, 23 per cent. He was not tested with bread.

It is quite possible that the slightly lower combustion of carbohydrate indicated by the quotients on the first as compared with the

TABLE 8.—INDIRECT

Subject and Date	Character of Experiment	Calories per Kg.	Average Calories per Hour		Per Sq. M., Linear
			Per Sq. M., Meeh	Per Cent. from Average Normal, 34.7	
Gerald S.					
11/ 9/14	Basal..........................	1.26	35.6	+ 2	36.7
11/12/14	Basal, second day of fast.....	1.38	38.3	+11	39.1§
11/14/14	Basal, fourth day of fast.....	1.32	36.4	+ 5	36.4
11/16/14	Basal, sixth day of fast.......	1.22	33.5	— 3	33.9
	Two hours after whisky.......	1.28	35.0	— 2	35.4
11/18/14	Basal, eighth day of fast......	1.08	29.5	—15	29.8
	Three hours after whisky......	1.15	31.7	....	32.0
11/20/14	Four hours after whisky......	1.11	30.2	....	30.7
11/23/14	Basal, fifth day of feeding....	1.00	28.5	—18	29.6
11/24/14	Basal, sixth day of feeding....	0.93	26.8	—23	28.0
11/25/14	Basal, seventh day of feeding	0.92	26.5	—24	27.7
	Two hours after whisky.......	0.98	26.7	....	28.0
11/30/14	Basal (with water drinking)...	0.99	28.5	—18	31.4
12/ 2/14	Basal..........................	1.02	29.5	—15	31.0
	Basal with exercise............	1.12	32.3	....	34.8
12/ 4/14	Exercise with basal............	1.07	30.6	....	32.7
12/ 7/14	Basal..........................	1.08	30.6	—12	31.8
William G. 1/11/15	Basal..........................	1.03	29.5	—15	29.3
1/15/15	Basal..........................	1.12	32.0	— 8	31.9
1/22/15	Basal..........................	1.37	37.2	+ 7	35.5
Joseph U. 2/1/15	Basal..........................	0.92	25.6	—26	25.4
Edward M. 10/30/14	Basal..........................	1.03	33.6	— 3	....
10/31/14	Two to five hours after 97 gm. olive oil	1.10	35.0	....	....
11/ 5/14	Two to five hours after 96 gm. olive oil following breakfast	1.29	40.9	+17	....
Felix K. 2/11/14	Basal after 1 green day........	1.19	37.3	+ 7	....
2/12/14	1¼ to 4¼ hours after 125 gm. oatmeal, 15 butter	1.38	43.4	....	....
2/14/14	1¼ to 4¼ hours after 125 gm. oatmeal, 15 butter; third oatmeal day	1.29	40.4	....	....
2/24/14	After 18 gm. bread and 9 butter every two hours	1.18	37.3	....	....
2/26/14	Basal..........................	1.13	35.8	+ 3	....
3/13/14	After 13.6 oatmeal and 9 butter every two hours	1.12	35.4	....	....
3/18/14	1½ to 5½ hrs. after 168 bread and 15 butter, 3d bread day	1.18	37.4	....	....
3/20/14	Basal after one green day.....	1.06	33.5	— 4	....
John O'C. 4/28/15	After 100 gm. oatmeal and 20 butter, first oatmeal day	1.45	37.0	(+ 7)	37.7
4/30/15	After same food, third oatmeal day	1.38	36.7	(+ 3)	36.7

* On account of respiratory quotient, dextrose-nitrogen ratio assumed to be 1.53 for purpose of calculation.
† Nonprotein respiratory quotient assumed 0.707 for calculations.

CALORIMETRY SUMMARY

Per Cent. from Average Normal 39.7	Average R. Q.	Average Non-protein R. Q.	Per Cent. Cal. from Carb.	Per Cent. Divergence of Direct from Indirect Cal.	Average Pulse	Remarks
— 8	0.719	0.707*	0	+ 2	75	Very quiet; D.-N. 1.53?*
— 1	0.697	0.700§	0§	— 2§	100	Asleep; D.-N. 3.5
— 8	0.702	0.68 †	0	— 8	80	Asleep; D.-N. 1.0
—15	0.710	0.701	1	— 1	..	Asleep; D.-N. 1.55
....	0.717	0.710	6	— 1	70	Asleep; D.-N. 1.55
—25	0.716	0.701	0	—21	..	Asleep; D.-N. 0.33
....	0.737.	0.727	6	+ 6	71	Awake; D.-N. 0.33
....	0.748	0.739	10	+ 1	61	Dozed
—26	0.727	0.712	2	—11	49	Awake
—29	0.758	0.744	10	— 9	51	Quiet
—30	0.764	0.756	14	—14	48	Dozed
....	0.726	0.712	1	—14	51	Dozed
—21	0.749	0.740	10	— 7	55	Quiet
—22	0.757	0.750	13	—16	56	Quiet
....	0.765	0.760	16	+ 2	56	Flexed arms 10 min.
....	0.760	0.753	13	— 2	59	Flexed arms 10 min. in first two periods
—20	0.759	0.753	15	— 2	55	Quiet
—26	0.741	0.732	7	— 4	61	Quiet
—20	0.707	0.714	0	— 6	68	Very quiet, dozed; D.-N. 3.8‡
—11	0.692†	0.693	0	— 7	64	Quiet; D.-N. 3.12
—36	0.743	0.733	8	— 3	72	Very quiet
....	0.805	0.806	28	—11	53	Fairly quiet
....	0.789	.....	....	— 5	59	Fairly quiet; urine lost
....	0.753	0.740	8	— 4	69	Quiet; breakfast at 7 a. m., Prot. 44, fat 204, Carb. 88
....	0.749	0.741	10	— 4	69	Fairly quiet
....	0.766	0.755	18	+ 1	77	Fairly quiet
....	0.817	0.820	32	+ 3	81	Fairly quiet
....	0.791	0.793	26	+ 7	72	Quiet
....	0.787	0.786	24	+11	74	Very quiet
....	0.781	0.770	15	+ 7	76	Asleep one half exper.
....	0.811	0.812	31	+ 2	70	Fairly quiet
....	0.768	0.762	18	+ 0	60	Quiet
(— 5)	0.772	0.763	14	+ 3	64	Fairly quiet
(— 8)	0.784	0.782	23	— 1	69	Fairly quiet
				Av. ± 5.5		

‡ D:N ratio assumed to be 3.65 for calculations.
§ Calculated from total O_2 and CO_2 for three hours.

third day of carbohydrate diet may indicate storage of glycogen after impoverishment on the preceding vegetable day, in harmony with the observations of Johansson and others on this point. The experiments fail to confirm Falta's conception of a striking difference in the manner of utilization of carbohydrate by diabetics on the first and third days of such a "cure." It would be desirable also to have information concerning the behavior of a normal subject under the same conditions, but such an experiment was not included in the present series.

Carbohydrate and water retention: The quantities of carbohydrate not accounted for by combustion are in all these experiments such as may easily be assumed to be stored as glycogen. The experiments are not of a character such as to throw light on the fate of carbohydrate under circumstances when, as Joslin[6] reckons, as much as 520 gm. may be retained and not accounted for by differences in the respiratory exchange. The fate of carbohydrate under these conditions must be regarded as not definitely settled. Glycogen storage is known to be commonly associated with water retention. Aside from the edema which authors have shown to be attributable to sodium chlorid and bicarbonate, the gain in weight of some diabetics during the oatmeal treatment may be related to the carbohydrate retention. It will be noted that the patient John O'C. actually gained about a kilogram in weight during the oatmeal period. On the other hand, Felix K., with a larger carbohydrate intake and apparent storage, gained no weight during his oatmeal period and lost a trifle during the bread period. This result therefore stands in marked contrast to the well-marked increase in weight which ordinarily occurs when a normal person changes from carbohydrate-poor to carbohydrate-rich diet.

2. *The Dextrose-Nitrogen Ratio.*—The cases of interest in this connection are those of William G., Gerald S., and that of Cyril K., which was described by Geyelin and DuBois; also another case more recently observed, a description of which will be published shortly by Gephart, Aub and DuBois.

William G., as previously stated, at first upon admission to the Presbyterian and Rockefeller Hospitals was found to show a dextrose-nitrogen ratio of approximately 3, with a strongly negative nitrogen balance. Table 4 contains his record six months later, during a period of feeding in the attempt to improve his strength. Starting with sugar-free urine on January 11, increase of protein and fat in the diet produced prompt glycosuria, with dextrose-nitrogen ratios higher than before. At least on January 15 and 20 the ratio was that of "total" diabetes. The actual quantities of both sugar and nitrogen excreted were less than in the former period when the ratios were smaller; and the nitrogen deficit was less although the diet was lower than before in both protein and calories. The clinical condition changed so rapidly

for the worse and the patient on January 22 was so ill and drowsy that it was necessary to resort to fasting to avert coma.

In Gerald S. the dextrose-nitrogen ratio was confused by the presence of carbohydrate in the diet until November 11. On this day no food was taken except 50 c.c. cream at 6 a. m. The ratio for the twenty-four hours November 11-12 was 3.68. The excessive nitrogen excretion which was a prominent feature with William G. was absent here. The fall in both glycosuria and ratio during fasting is evident from Table 2.

Cyril K., the patient of Geyelin and DuBois, fasted five days without abatement of any of the diabetic symptoms, and with acidosis steadily increasing either because of the fast or in spite of it. Then, on account of dyspnea and drowsiness threatening coma, he was given low diet for a few days, consisting chiefly of protein, though containing also 53.3 gm. carbohydrate December 14 and 23.5 gm. December 15. The dextrose-nitrogen ratios for the next three days (December 15 and 17 inclusive) were 3.97, 4.01, and 3.87. The nitrogen loss at this period was greater than ever before described in uncomplicated diabetes. Beginning December 17, the condition gradually yielded to the second fast-treatment, as indicated by the fall of sugar, nitrogen, the ratio and the acidosis.

The case of Gephart, Aub and DuBois appeared at first to be of no extreme severity, and the urine was readily cleared up by fasting. Thereafter, in consequence of excessive protein-fat diet and the simultaneous development of an alveolar abscess, glycosuria suddenly appeared, and by the second day the 3.65 ratio was attained. The condition then yielded promptly to a repetition of fasting.

It is desirable here to discuss the dextrose-nitrogen ratio as respects (a) its occurrence in human diabetes, (b) its practical and (c) its theoretical significance.

(a) Lusk has insisted that trustworthy ratios are obtainable only when the diet contains no appreciable quantity of carbohydrate. The examples in the entire literature are very few, largely because the type of patients most likely to show the maximum ratio has so seldom been subjected to the conditions necessary to establish the ratio. Foster[28] says: "The diabetic patient is for several reasons an extremely difficult subject for these experiments. It is usually impossible to restrict him for a period of a week to a fat-protein diet." Benedict and Joslin[4] mention the danger of placing a patient with severe diabetes upon a strict protein-fat diet for several days. Joslin[5] also calls attention to possible errors due to excretion of retained carbohydrate unless ade-

28. Foster, N. B.: Diabetes Mellitus, Lippincott Co., Philadelphia and London, 1915, p. 30.

quate precautions are taken. The conditions involved in fasting differ in some respects from those of protein-fat diet. Though sometimes an existing ratio of 3.6 rapidly diminishes on fasting, and the glycosuria clears up, in other cases this ratio is clearly developed and persists for at least several days. Since the introduction of the fasting treatment, examples, mostly unpublished as yet, of such a ratio have been observed by several clinicians. It is probable that such observations will henceforth be made more frequently, not because the incidence of such "total" diabetes is increased by the fasting treatment, but because this method involves placing severely diabetic patients as a routine measure upon a program of complete carbohydrate abstinence for considerable periods, thus facilitating demonstration of the ratio with freedom from previous difficulties and errors. This is one of the features in which the new treatment has proved of service not merely for the practice, but also for the theory, of diabetes.

(b) Recent experience confirms the suggestion of Lusk[18] that the presence of the above-mentioned ratio need not be permanent or carry a rapidly fatal prognosis. In the patient as in the phlorhizinized animal, the relation between sugar and nitrogen in the urine under suitable conditions is an index of the deficiency of carbohydrate combustion, and the maximal ratio shows total absence of utilization of the sugar formed from protein. This ratio does not necessarily indicate the highest possible quantity of protein catabolism or sugar excretion. The nitrogen excretion of Gerald S. was never high. William G. showed markedly excessive protein destruction at first; later (January 15) the ratio was maximal, but the protein breakdown moderate. Cyril K., as above remarked, showed the most rapid nitrogen loss ever recorded in a case of diabetes, and this loss was still excessive on December 22-23, when the ratio had fallen to 1.12. Phlorhizin given to Gerald S. could not have increased the ratio but would perhaps have increased the quantities of sugar and nitrogen excreted.[29] The reason for the remarkable intensity of protein catabolism in some cases is not known. There is no justification for the term "toxic" applied by Magnus-Levy and others. So far as existing data permit judgment, the difference does not lie in acidosis, for the patients mentioned seemed about equally close to coma. The bodily strength and nutritive state may play a considerable part. For example, Cyril K. (Geyelin and DuBois), with recent acute diabetes, had the necessary strength and reserves for intense waste of sugar and nitrogen, like the typical experimental animal. Gerald S. was weak and emaciated. William G.

29. This remark applies to fasting. On liberal protein-fat diet Benedict and Lewis (The Influence of Induced Diabetes on Malignant Tumors, Proc. Soc. Exper. Biol. and Med., 1914, xi, 134), found the nitrogen excretion of human subjects not increased by "total" phlorhizination (personal communication).

was weaker in the second of the periods described than in the first, and weighed some 5 kg. less. But this may not be the whole explanation. A specific disorder affecting protein metabolism in some patients, as in totally depancreatized dogs, is not excluded. The possibility of very rapid changes in the ratio, as exhibited most strikingly by the patient of Gephart, Aub and DuBois, is one of the strongest evidences in favor of the functional element in human diabetes. Such sudden changes for the worse or for the better are scarcely to be expected in the case of purely organic lesions, and are contrary to the results in animals when the islands of Langerhans have been lost. Because of the generally more favorable outlook for functional as opposed to organic disturbances, the dextrose-nitrogen ratio therefore contributes something to the prognosis in human diabetes. For the very reason that the process is at least partly functional and under appropriate treatment may be temporary, the dextrose-nitrogen ratio fails to define the later prognosis in any individual case. Aside from the duration of the trouble and other fallible clinical indications, there is now no basis for predicting which patients are likely to recover tolerance quickly and in considerable degree, and which are likely to improve slowly and in slight measure. Experience to date indicates that cases of brief acute course, when checked by radical treatment, may show a correspondingly more rapid improvement as compared with the more protracted cases in patients of corresponding age and type. The occurrence of the dextrose-nitrogen ratio of the phlorhizinized dog in any human patient may be taken as a sign of the gravest immediate significance. The few known to have exhibited this ratio during fasting have died, except the patient of Geyelin and DuBois. The exception is believed to be due to the skilful alternation of fasting and protein feeding in this case, but further experience will be necessary for decision. It is at least established that careful treatment offers some hope even in cases of this type, and that with the worst of ratios and other symptoms an appreciable carbohydrate tolerance may subsequently be regained.

(c) The principal debate concerning the dextrose-nitrogen ratio has been not whether values as high as those mentioned occur in human patients, but whether any higher values ever occur. Animal experiments aiming to prove the formation of sugar from fat have all miscarried; but a few authors still hold that occasional cases of exceptionally severe human diabetes show dextrose-nitrogen ratios so high as to be explainable only by the formation of sugar from fat. Some of the cases above described are not lacking in severity, but rather give the impression of being more severe than those in the literature in which sugar was supposed to have been formed from fat; and neither on protein-fat diet nor on fasting were any ratios observed which could justify the assumption of sugar-formation from fat. It may be argued

that the negative evidence in the present cases cannot overthrow positive evidence in other cases, which though not more severe may have been of peculiar character. Alone, it could not do so. But the carbohydrate hunger of patients on old-fashioned protein-fat regimen caused numerous writers to compare them to drug addicts with respect to their ingenuity, pertinacity and also mendacity in obtaining forbidden food, even when supposedly isolated and watched; and experienced observers are aware that only special environment and special qualifications of the nurse in charge can guarantee against this source of error. As accuracy of investigation has increased, the number of reports of ratios indicating sugar formation from fat has diminished. Apparently no such ratio has ever been described in America; and the experience of the majority of clinics and laboratories elsewhere is similar. The justification for questioning the alleged findings in occasional cases at a few European clinics is found in the large number of accurate observers who see numerous diabetics of various grades of severity, but are still waiting to see any case showing the excessive ratios mentioned. The general agreement of negative evidence is believed now sufficient to set aside the principal support of the doctrine of sugar formation from fat, namely, the supposed occurrence of this process in diabetic patients.

3. *The Respiratory Quotient.*—In the cases mentioned, except that of Cyril K., the Lusk dextrose-nitrogen ratio was present only for brief periods. The objection might therefore be raised that these ratios were purely accidental, and partly accounted for by sweeping out of more or less carbohydrate previously retained as glycogen or sugar. Here the necessary proof is afforded by the respiratory quotients. In the case of Gerald S. it was impossible to determine accurately the dextrose-nitrogen ratio November 9, the day after a considerable amount of carbohydrate in the food, so it was assumed for purposes of calculation to be 1.5, a figure which gave theoretical results. On the second day of the fast, the dextrose-nitrogen ratio being 3.5 during the calorimeter period, the total quotient was 0.697 and the nonprotein quotient 0.7. On the sixth and eighth days of the fast the nonprotein quotients were 0.701 and 0.701 respectively. For William G. in the last two experiments (January 15 and 22), with dextrose-nitrogen ratios of 3.81 and 3.12 during the calorimeter periods, nonprotein quotients of 0.714 and 0.693 were found. The average nonprotein quotient on all these days was 0.703, as compared with the theoretical figure of 0.707 for fat. These and the similar quotients observed in Cyril K. serve to show that the dextrose-nitrogen ratios obtained under the above conditions were not accidental, but at the times when the Lusk ratio was present the diabetes was actually "total." These quotients also agree with the results of Benedict and Joslin and other exact work in fur-

nishing additional testimony against the formation of sugar from fat, thus fully confirming the evidence afforded by the dextrose-nitrogen ratio.

The tables also show that during the fasting treatment the power to oxidize carbohydrate gradually improved, as would be expected from the urinary findings. On fasting and on low diet thereafter the patients were able to derive an appreciable percentage of the energy requirement from this source. Joseph U. was able thus to derive 8 per cent. of his requirement. Gerald S., from a condition of total inability to oxidize sugar, apparently became able to derive 15 per cent. of his energy from it. William G. illustrated the opposite change produced by protein-fat overfeeding. January 11, on low diet, he was deriving 7 per cent. of his requirement from carbohydrate. The protein and fat were then increased, and by January 15 "total" diabetes was present.

Brief mention may also be made of the two exercise experiments with Gerald S. on December 2 and 4. The exercise performed in the calorimeter consisted in flexing and extending the forearms for ten minutes at the beginning of a period. The labor performed was sufficient to raise the heat production by 18 per cent. for the hour period, or by about 100 per cent. for the ten minutes of actual exercise. The respiratory quotient showed no change during this hour, remaining at 0.75; but in the next hour the total quotient was 0.779 and the nonprotein quotient 0.77, which figures are higher than the averages obtained in any of the experiments with this patient at rest. On December 4 a similar ten minutes of exercise was inserted at the beginning of the preliminary period, immediately after the calorimeter was sealed, and also at the beginning of the first and second hours thereafter. The quotient in the first hour was 0.778, corresponding to that on December 2; the quotient in the second hour was lost through accident. The experiments at least give no indication of a lowering of the quotient due to any hypothetical exhaustion of glycogen in a patient supposedly glycogen poor. This aspect is to be emphasized more than the slight rise of the quotient, which might have been accidental in the two experiments, though it may perhaps suggest a slight increase in carbohydrate utilization, possibly bearing some relation to the therapeutic benefits of exercise.[9]

The most surprising feature pertaining to the respiratory quotients consisted in some unexpectedly high values obtained, similar to those described by Joslin. For example, Gerald S. fasted eight days, November 11 to 19, then received a gradually increasing protein-fat diet, with from 750 to 1,000 gm. of thrice-boiled green vegetables daily. On the fifth day of this diet, November 23, the quotient indicated that he was deriving 2 per cent. of his calories from the combustion of carbohydrate. The subsequent experiments, up to December 7, gave quo-

tients indicating combustion of between 10 and 15 per cent. carbohydrate, with an average of 12 per cent. During this period the basal metabolism averaged 1,042 calories per twenty-four hours. If he were deriving 12 per cent. of his calories from carbohydrate, he must have metabolized an average of 31.3 gm. a day or a total of 438 gm. in the two weeks. According to the analyses of the thrice-boiled green vegetables, which were the only possible source of starches or sugars, he could not have received more than 2 or 3 gm. of carbohydrate a day. It is improbable that he could have maintained a store of 400 gm. of glycogen in his body under the circumstances. The blood sugar did not fall enough to suggest that more than a small fraction could have been derived from this source, and the recent work of Palmer[30] proves, as far as is possible with animal experiments, that the quantity of sugar present as such in the tissues is insignificant. The results after the ingestion of whisky are also hard to interpret. It is known that alcohol requires a moderate amount of time, sometimes several hours, for its complete combustion, but it is impossible to tell how much alcohol is metabolized each hour, since the nonprotein respiratory quotient will not solve a problem with three unknowns. Alcohol has a quotient of 0.667, but it may possibly cause vasomotor and respiratory changes leading to an elimination or retention of carbon dioxid with resulting false quotients. But its action in normal persons or animals is to depress the quotient; in all the extensive studies concerning the utilization and effects of alcohol, a rise of the quotient after its ingestion has never been reported. In the earlier whisky experiments with Gerald S., there was a sharp rise in the quotient after drinking, followed by a corresponding fall in the second hour, the highest non-protein quotients for single hours being 0.764 on November 18, and 0.773 and 0.782 on November 20. This was not seen in control experiments in which the patient drank the same amount of plain water at the same temperature, or went through the movements of drinking without swallowing any liquid. Mild exercise, as above stated, had no immediate effect on the quotient. Finally, on Nov. 25, the whisky was given in such a way that there was absolutely no exertion on the part of the subject, and although the rise of quotient in the first hour was absent, the marked drop in the second hour was present. In this last observation there was no apparent increase in the combustion of carbohydrates, but in the first three the average quotient of the hours after whisky was slightly higher than before. There was thus an apparent increase in the carbohydrate metabolism, which would be even higher than calculated if alcohol with its low quotient were oxidized, thus tending to lower the total quotient.

Joslin has suggested that combustion of retained acetone bodies, with their high quotients (beta-oxybutyric acid 0.89, diacetic acid 1.00),

30. Palmer, W. W.: In press.

may account for some rise in the quotients of these patients. The suggestion is supported by the observation that on fasting the ketonuria falls and the quotient rises. Also, if it should prove true that alcohol diminishes ketonuria, as claimed by authors[31] in the past, the rise of the quotient after ingestion of alcohol might correspond to an increased combustion of acetone bodies. The high quotients as described seem to be a regular or frequent phenomenon in patients with severe diabetes under the conditions described, and the possibilities may be discussed by comparison of the cases reported. The blood sugar, as stated, fell somewhat in the case of Gerald S., but rose during the development of the increased quotients in Geyelin and DuBois' patient (Cyril K.), and in the patient of Joslin.[19] The above calculation in the case of Gerald S. requires the equivalent of 400 gm. of glycogen to explain the quotients observed. No patient could possibly retain enough acetone bodies to correspond to the whole of this requirement. The high quotients have generally been observed when the glycosuria and ketonuria were diminishing either during or after fasting, or on ingestion of whisky. An exception is present in the case of Cyril K. when receiving protein diet on December 16-17. Here the ketonuria was higher than on any previous day, namely, 75 gm. reckoned as beta-oxybutyric acid. The carbon dioxid capacity of the blood plasma had fallen to its lowest point, namely, 19.6 (the normal figures being from 40 to 45). The dextrose-nitrogen ratio was at its highest point, namely, 4.01. Under these circumstances it is difficult to understand what kind of material could be burned to give the observed nonprotein respiratory quotient of 0.743. This single result may possibly be due to some accident connected with the circumstances of this particular case. On the other hand, it may possibly be of some significance in connection with the fact that, although all the laboratory tests aside from the respiratory quotient indicated that the patient was in no wise better and in some respects worse on December 16-17 than on December 9-10, yet it was evident clinically that his condition was much better on the latter date and the symptoms of intoxication greatly diminished. This patient was receiving alkali during this period, but Gerald S. and Joslin's patient received none; therefore the quotients can scarcely be due to dosage with bicarbonate. It is conceivable that high quotients in one part of the twenty-four hours might be compensated by low quotients in another part. No respiration experiments were performed at night, but it is scarcely probable that any marked difference existed between

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31. Neubauer, O.: Ueber die Wirkung des Alkohols auf die Ausscheidung der Azetonkörper, München med. Wchnschr., 1906, liii, 791. Benedict, H., and Török, B.: Der Alkohol in der Ernährung der Zuckerkranken, Ztschr. f. klin. Med., 1906, lx, 328. Stäubli, C.: Beiträge zur Pathologie und Therapie des Diabetes mellitus, Deutsch. Arch. f. klin. Med., 1908, xciii, 107.

day and night. Such a difference would in itself constitute an abnormality, for the day and night quotients have never been known to vary to such an extent in previous experiments on normal persons and animals. It is noteworthy that while the average divergence between the methods of direct and indirect calorimetry in the present series was only 2.3 per cent., and the agreement was close in the first experiments with Gerald S., yet beginning with the eighth day of his fast, November 18, when the period of high quotients began, there appeared minus errors of the direct as compared with the indirect calorimetry sometimes as high as 21, 14 and 16 per cent. Such discrepancies might in part be explained if the quotients were due to combustion of some other material, perhaps acetone bodies, instead of carbohydrate as assumed, for then the reckoning of the indirect calorimetry would be considerably altered. On the other hand, the divergence may possibly have been due to technical error in the measurement of the average temperature of the body.

4. *The Total Metabolism.*—In regard to the general question of heat production the present series of experiments agrees with the work of previous authors in showing the basal metabolism per kilogram of body weight to be increased in severe diabetes. But as above mentioned, the principal need in connection with this vexed question has been a satisfactory standard of comparison between diabetic and non-diabetic subjects. The linear formula devised especially to throw light on this subject is believed to afford such a standard, and the conclusions in the present paper are drawn on the basis of this mode of calculation. The summary in Table 8 shows that the surface area of thin diabetics is not so much smaller than that of normal men as would be indicated by Meeh's formula, and consequently their metabolism is considerably lower when compared with the normal average according to the linear or height-weight formula than when Meeh's less accurate formula is used. The difference between the results as expressed in terms of the two formulas in the case of Gerald S. is from 8 to 13 per cent. With William G. it is from 11 to 18 per cent., with Joseph U., 10 per cent., with John O'C., from 11 to 12 per cent. These were all very thin diabetics, and the differences with less emaciated patients would be proportionately smaller. With patients stouter than the average the metabolism would be higher according to the linear formula than according to Meeh's, but patients with severe diabetes are seldom stout.

Among the patients described in the present paper, it was noted that Gerald S. entered the hospital in a weak and exhausted condition. His metabolism at this time, November 9, was 2 per cent. above the average normal by Meeh's formula, but 8 per cent. below the average normal by the linear formula. William G. had been subjected to

prolonged low diet. Starting at 26 per cent. below normal on January 11, when glycosuria was absent, his metabolism rose, on increased diet and the return of active diabetes, to 20 per cent. below normal on January 15 and to 11 per cent. below normal on January 22. On the other hand, in the patient of Geyelin and DuBois[26] (Cyril K.), the diabetes was recent and acute, and here the metabolism was above normal. The respiration experiment on December 15 was after food, therefore the metabolism of 15 per cent. above normal does not represent a true basal value. The highest basal metabolism actually demonstrated here was 3 per cent. above normal on December 18.

The patient Edward M. never showed the true ravenous hunger of diabetics, but had been a heavy eater all his life and could dispose of a large diet exceptionally well, with no increase of his slight dyspeptic complaints. During most of September, weighing 58 to 63 kg. and leading the inactive life of a ward patient, he had enjoyed a high diet, the maximum being during the period September 21 to 26, with from 6,100 to 6,300 calories daily, consisting chiefly of fat, of which there was nearly 600 gm. daily. Instead of steatorrhea, there were small constipated stools, showing exceptionally high utilization by analysis. As stated in his history, the diet had been moderate but adequate preceding the first calorimeter tests. The body weight was about 60 kg., as opposed to his original "normal" weight of about 80 kg. But he felt well and strong at this weight, and, correspondingly, the basal metabolism on October 30 was found entirely normal, 3 per cent. below the average. On October 31 the metabolism was measured two to five hours after drinking 97 gm. olive oil. Table 8 shows the resulting increase of metabolism and lowering of the respiratory quotient. On November 3 the diet contained 5,300 calories with 483 gm. fat, and on November 4, 5,268 calories with 482 gm. fat. On the morning of November 5 the patient entered the calorimeter after taking 44 gm. protein, 38 gm. carbohydrate and 204 gm. fat. The metabolism two to five hours afterward is shown by Table 8 to average 17 per cent. above normal. Accordingly, the specific dynamic action of food, especially of fat, did not differ noticeably from the normal as respects its promptness or intensity in this patient, and there was no indication of an abnormally high metabolism ("Luxuskonsumption") on the excessive diet. The result with this patient under the conditions does not warrant a positive conclusion concerning possibilities in more severe cases, especially at the height of the diabetic process.

Since the last important discussion of the total metabolism in diabetes by Benedict and Joslin there have been several changes in the general point of view of the metabolism of normal controls and of diabetics as the result of work presented in previous papers of this series. In the light of these it has seemed advisable to recalculate the

cases of severe diabetes reported in the literature, and discuss the question in its most recent aspects. As we have shown, it is advisable to abandon comparisons made on the basis of cubic centimeters of oxygen per kilogram and minute and use instead the calories per square meter per hour. Recent work on the metabolism at different ages has emphasized the fact, first brought out clearly by Magnus-Levy and Falk,[32] that metabolism changes with age. It must be remembered that a study of the surface area designed primarily to afford a basis of comparison between patients and normal controls has shown that Meeh's formula is not so accurate as the newly devised linear and height-weight formulas. Most important of all has been the study of a large number of controls by Benedict, by Means[33] and by the Russell Sage Institute staff, giving a normal basis of comparison which is not influenced by variations that might occur in small groups or by single investigators.

In Table 9 are given the results obtained in a large number of cases of severe diabetes. Since the height-weight formula was employed as a basis of comparison, the only cases that could be used were those where the height was given. This unfortunately has prevented the recalculation of the severe cases of Leo,[34] Nehring and Schmoll,[35] Rolly,[7] and some of the cases of Magnus-Levy[14] and Mohr.[36] The work of Leimdörfer[17] has not been recalculated, since the abnormally low quotients make this impossible, nor has the work of Grafe and Wolff,[37] where it is difficult to reconcile the high respiratory quotients and high dextrose-nitrogen ratios. As will be seen, the large majority of cases was furnished by the careful work of Benedict and Joslin. For purposes of comparison, columns have been added showing the duration of life after the period of experimentation, the level of the nitrogen metabolism, the degree of emaciation, and the estimated degree of acidosis. If we study first the column showing the percentage variation from the normal, it will be noted that out of twenty-six cases thirteen are within the normal range of plus or minus 10 per cent. from the average. There are nine patients with an increase

32. Magnus-Levy, A., and Falk, E.: Der Lungengaswechsel des Menschen in den verschiedenen Altersstufen, Arch. f. Physiol., 1899, Suppl., 314.

33. Means, J. H.: Basal Metabolism and Body Surface, Jour. Biol. Chem., 1915, xxi, 263.

34. Leo, H.: Ueber den respiratorischen Stoffwechsel bei Diabetes mellitus, Ztschr. f. klin. Med., 1891, xix, Suppl., 101.

35. Nehring, O., and Schmoll, E.: Ueber den Einfluss der Kohlehydrate auf den Gaswechsel des Diabetikers, Ztschr. f. klin. Med., 1897, xxxi, 59.

36. Mohr, L.: Untersuchungen über den Diabetes mellitus, Ztschr. exp. Path. u. Ther., 1907, iv, 910.

37. Grafe, E., and Wolf, G. L.: Beiträge zur Pathologie und Therapie der schwersten Diabetesfälle, Arch. f. klin. Med., 1912, cvii, 201.

of from 11 to 23 per cent. and these deserve special attention. Two of these, V. and Cyril K., were studied after food, and if the stimulus of the recent meal were removed they might have come within normal limits. One of the subjects, G., was under intense nervous excitement during the experiment, and another, I., with a pulse of 120, had been described the year before as very nervous. This leaves us five cases in which there was a moderate but distinct rise in the metabolism, namely, Herr Mo., Frau Schm., Frau St., H., and U. To these we should perhaps add Cyril K. at the time of his first experiment, when after a breakfast his metabolism was 15 per cent. above the normal basal. To offset these there are four patients whose metabolism ranged from 14 to 19 per cent. below the average. Three of these, N., P. and Q., were children, and it is quite possible that the normal stimulus of the growing organism was checked by the diabetes. The fourth subject, Wm. G., was extremely emaciated. If we take the algebraic mean of the 26, we find that the metabolism in severe diabetes averages 3.3 per cent. above the normal, a figure which might be increased to about 5 per cent. by taking into account the fact that the average for the 89 normal controls of Benedict is 2 per cent. lower than the Sage standards.

Benedict and Joslin[4] found that the average oxygen consumption of their diabetics per kilogram and minute was 15 to 20 per cent. above that of their twenty normal controls. Part of this difference was due to the fact that at that time few investigators realized the importance of the age factor. Part was due to the unusually low metabolism of the normal controls. In the twenty controls used by Benedict and Joslin for comparison with the diabetics, there are seven whose metabolism is 10 per cent. or more below the average normal described in the previous papers of this series. It so happens that these seven, A. F. G., T. M. C., Dr. P. R., Dr. S., H. F. T., E. P. C., Mrs. S. C., are used seventeen times in the total column of thirty-two, making the average of the column 8.6 per cent. below the standard. This is much greater than the divergence of —2 per cent. found in the total of eighty-nine normal controls. Their cases with severe diabetes, recalculated in terms of the height-weight formula, average only two per cent. above the Sage normal standard. It would appear that the metabolism of Benedict and Joslin's diabetic patients is within normal limits, while the large difference between their pathologic and normal cases is due chiefly to the low metabolism of the subjects selected for normal controls. It is quite possible that the low metabolism of these controls was due to the fact that they were poorly nourished and were selected because they resembled diabetics in this respect.

TABLE 9.—THE BASAL METABOLISM OF PATIENTS WITH SEVERE
SURFACE AREA AS ESTIMATED BY

Investigator	Subject	Sex	Age, Yrs.	Calories per Sq. M. per Hr. Height-Weight Chart	Normal Standard Cal. per Sq. M. per Hr. for Same Age and Sex	Per Cent. Variation from Normal Standard	Respiratory Quotient, Average
Magnus-Levy	Herr Mo.	♂	43	46.9	39.7	+18	0.70
	Frau Schm.	♀	35	41.2	36.9	+11	0.72
Mohr	Frau St.	♀	52	40.5	32.7	+23	0.71
Benedict and Joslin	A	♂	50	36.6	35.2	+ 4	0.71
	B	♀	40	36.0	36.9	− 2	0.73
	C	♂	28	40.1	39.7	+ 1	0.70
	D	♂	39	36.9	39.7	− 7	0.74
	G	♂	35	45.1	39.7	+14	0.73
	H	♀	38	40.9	36.9	+11	0.77
	I	♂	25	45.2	39.7	+14	0.73
	J	♂	20	43.6	39.7	+10	0.76
	K	♂	46	39.1	39.7	− 2	0.72
	L	♂	23	43.5	39.7	+10	0.73
	N	♂	14	43.0	49.9	−14	0.74
	O	♀	16	37.9	39.0	− 3	0.72
	P	♂	15	39.7	49.0	−19	0.69
	Q	♂	14	42.2	49.9	−15	0.77
	R	♂	47	43.6	39.7	+10	0.72
	S	♂	57	34.2	35.2	− 3	0.73
	T	♂	44	39.6	39.7	0	0.73
	U	♀	37	42.4	36.9	+15	0.73
	V	♂	36	45.8	39.7	+15†	0.73
Geyelin and DuBois	Cyril K. Dec. 15 & 16	♂	21	44.2	39.7	+11†	0.70
	Dec. 18	♂	21	40.8	39.7	+ 3	0.71
Authors	Gerald S. Nov. 9 & 12	♂	17	39.7	39.7§ (42.0*)	− 5 (−10*)	0.71
	William G. Jan. 15 to 22	♂	29	33.7	39.7	−15	0.70

* Using average normal for age of 17.
† Part of increase due to recent food.
§ Using average normal for ages 20 to 50.

Diabetes Compared with Normal Standards According to the the "Height-Weight" Formula

Time Before Death in Months	Urine N per Day, Gm.	Emaciation or Per Cent. of Loss from Greatest Weight	Degree of Acidosis	Remarks B = Beta-oxybutyric Acid per Day
Coma 2	.....	++	++?	
Coma 6	.....	++	++?	
....	.....	.....	±	Moderately severe; Diac. 0 to +
Tb. 20	6-14	Per Ct. 10-18	+	NH_3N 3.3, Diac. +, Active Tb. in lungs
Coma 6-1	.....	9-18	++(?)	Diac. ++++
Coma 2	13-22	14-24	+++	B 14 to 61; NH_3N 2.6 to 5.6
Coma 3	13	15	0:+	Diac. 0 to ++++, urine alk. with 8 to 45 sod. bicarb.
Coma 15	17	+	+++	B 30, NH_3N 4.2, Diac. +++++, intense nervous excitement during experiment
Coma 4	9-12	14	+	B 8 to 11, Diac. 0 to +
15	14	30	±	B 4.8, NH_3N 2.2, pulse 120 (nervous?)
36	.....	15	±	Diac. + to ++, nervous temperament
Coma 16-4	16-20	20-24	0:++	B 30, Diac. 0 to ++, NH_3N 3 to 5.8
Alive	.....	20-16	±	Diac. 0 to sl. +
Coma 1½	5-10	9	+++	B 21 to 30, Alv. CO_2 Hald. 16 to 28
Coma 3	8-11	14	+	B 13 to 14
Coma 1	5-18	20	+++	Diac. ++++, NH_3N 4.6 to 5
Coma 4	7-14	5	++	B 20 to 27, NH_3N 2.2 to 4.6, Alv. CO_2 31 to 40
Tb. 10	13-16	17	++	B 42 to 50, NH_3N 5 to 6, somewhat nervous, moved considerably
Coma 5	7.3	18	+	Diac. ++, NH_3N 1.2
Coma 1	9-12	28	+++	B 40 to 50, NH_3N 4.6 to 5.2, Boils
Coma 15-3	7-9.5	26	++	B. 18 to 22, NH_3N 3.6 to 4
Pneu. 11	.....	6	0	Diac. 0. After light breakfast
Alive	36-37	27	+++	B 71 to 75, blood CO_2 19.6 to 20 After large breakfast
Alive	20	27	+++	B 58, blood CO_2 35, second fast day
Coma 4	11-15	31	++	B 3 to 14, NH_3N 3.4 to 4.7
Coma Tb. 2	14-20	42	+	Diac. ++, NH_3N 3.4, B 0.1 to 1.3

The profound effect of confinement and undernourishment on heat production has never received the attention it deserves. The reduction of metabolism in fasting has been shown in several experiments, the best being the recent work of Benedict,[20] whose subject L. fasted thirty-one days. On the first day of the fast he produced 40.3 calories per square meter per hour as measured while awake in the morning and as calculated by the height-weight chart. This figure is 1.5 per cent. above the normal average for similar conditions. On the tenth day of the fast the metabolism calculated in the same way was 16 per cent. below the average, and it remained between 18 and 22 per cent. below during the rest of the fast. A similar or even greater lowering of metabolism results from prolonged undernutrition. The figures of Svenson and others[38] for emaciated typhoid convalescents when compared with the normal standard indicate a metabolism considerably below normal in some instances. By similar calculation, the results of Magnus-Levy[39] with a neurasthenic youth who partially starved himself for a long period, are as follows:

TABLE 10.—METABOLISM EXPERIMENT ON MAGNUS-LEVY'S PATIENT *

Period	Date	Condition	Calories per Sq. M. per Hour Height-Weight Formula	Weight, Kg.	Relationship of Metabolism to Average Normal 39.7
I	Nov. 16 to 21..........	Very low diet.........	26.6	36.2	—33%
II	Nov. 23 to Dec. 9.......	Liberal diet............	33.0	33.0	—17%
III	Jan. 26 to March 6.....	Fever from Tb.	43.4	48.4	+ 9%
IV	March 13 to May 8.....	Normal again.........	40.5	52.2	+ 2%

* Age 19, height 160 cm.

These figures are comparable to those shown in the present series of diabetic patients after treatment. The degree of elevation of metabolism due to the active diabetic process should be judged by comparison of such patients with equally emaciated and cachectic nondiabetics. It is also now possible to compare the same patient at times when active diabetes is present or absent, while the body weight and surface remain the same. Thus Gerald S., with intense diabetes, on November 9 had a basal metabolism 8 per cent. below normal. His fast ended November 18, and from then until December 7 he received a diet such that his

38. Recalculated in terms of surface area according to Meeh's formula, by Coleman and Du Bois, The Influence of the High Calory Diet on the Respiratory Exchanges in Typhoid Fever, THE ARCHIVES INT. MED., 1914, xiv, 168 (Fig. 4).
39. Magnus-Levy, A.: Der Einfluss von Krankheiten auf den Energiehaushalt in Ruhezustand, Ztschr. f. klin. Med., 1906, lx, 177.

weight on the latter date was practically identical with that on November 9; but the basal metabolism on December 7 was 22 per cent. below normal at a time when the urine was free from sugar. William G. weighed 43.2 kg. on December 11. In consequence of feeding high-caloric diet, the weight fell to 42 kg. by December 22, while the metabolism rose from 26 per cent. below normal on December 11 to 11 per cent. below normal on December 22. If we study Table 9 it is apparent that most of the diabetics with marked emaciation have a diminution in metabolism. In the children with diabetes and low metabolism the percentage loss from the greatest weight is small, but with a child that is growing taller even a stationary weight indicates emaciation. If "normal" adults and children were as emaciated as the diabetics, they would undoubtedly show a marked diminution in heat production.

Benedict and Joslin have ascribed an increase in diabetes to acidosis. This is usually associated with an increased protein metabolism, and it is often difficult to separate the two factors. It has long been known that increased protein metabolism causes an increased heat production. If we turn to Table 9 we can compare the increased metabolism with the degree of acidosis. There were nine patients whose metabolism was 11 to 23 per cent. above the normal. Of these two showed marked acidosis, namely, Cyril K. and the nervous patient G. Three others, Herr Mo., Frau Schm. and U., had severe acidosis. Patient H. had moderate acidosis, while the others, I. and V., had little or no acidosis, and the patient Frau St., with the highest metabolism of all, had very slight acidosis. In contrast to this, eight patients with severe or very severe acidosis showed a normal or decreased metabolism. These are B., C., N., P., Q., T., Cyril K. (December 18), and Gerald S.

Authors have erroneously attempted a direct comparison between dogs depancreatized or phlorhizinized at the height of their strength, and human patients who reach the stage of severe diabetes, generally after months of a slow cachexia. Accurate comparison demands equally acute human diabetes, or else the use of dogs with chronic diabetes or prolonged cachexia. The excessive nitrogen excretion of William G. and especially of Cyril K. (Geyelin and DuBois) is well comparable to that of the totally depancreatized dog, and in the latter the total metabolism was actually above normal in spite of four weeks of rapid wasting followed by five days of complete fasting. The alleged difference as respects increase of metabolism can therefore no longer stand as a distinction between clinical and experimental diabetes.

Theoretically it is to be expected that the metabolism will rise with the increase of the protein metabolism which accompanies the noncombustion of sugar derived from protein in the diabetic condition. Since the specific dynamic action is less in human beings than in dogs, it may

well be that the stimulus of an increased protein metabolism is relatively less pronounced in human than in experimental canine diabetes.

Recapitulating, one may state that the linear formula furnishes a more accurate standard of comparison than was previously available. According to calculation by this formula, an increase above the true normal metabolism is not demonstrable in the majority of patients with severe diabetes. Nevertheless, the diabetic process may be associated with a relative elevation of metabolism. In occasional instances the metabolism may actually exceed the average normal level of metabolism. In all cases the true increase appears only when one takes into consideration other factors incidentally present, some of them tending strongly to depress metabolism. For example, the percentage of increase may be fully as great as claimed by Benedict and Joslin, if the metabolism of diabetics is compared with that of other equally undernourished subjects, or if the same patient is compared at different times when active diabetes is present or absent. In practical application, the results indicate that diabetics generally have no higher food requirement than normal, and on account of undernutrition and lessened muscular activity will tend to maintain equilibrium on a smaller number of utilizable calories than normal persons. Because the diabetic is less active, as pointed out by Magnus-Levy, his actual consumption of energy as compared with normal controls is likely to be less. After treatment by fasting, even though the patient is gaining steadily in strength and well-being, a low level of metabolism has been observed, the lowest 36 per cent. below normal, and this indicates that a low diet will suffice for maintenance under these conditions.

SUMMARY AND CONCLUSIONS

1. Three patients with severe diabetes and three with moderate or mild diabetes have been studied in the respiration calorimeter. The effects of the oatmeal treatment and the fasting treatment have been followed in detail.

2. No special influence of oatmeal in diabetes or special readiness of oxidation of this form of carbohydrate was demonstrable in these experiments. The respiratory exchange fails to account for all the carbohydrate that disappears. The behavior of the respiratory quotient showed no important difference on the first day and on the third day of the oatmeal treatment.

3. The occurrence of "total" diabetes in human patients, with dextrose-nitrogen ratios approximating 3.65 to 1 and corresponding respiratory quotients, is here shown. Notwithstanding the extreme severity, neither the sugar excretion nor the gaseous exchange gives ground for assuming the formation of sugar from fat in any instance.

4. Even in the severest type of diabetes the active symptoms may

be eliminated completely by prolonged fasting. The observations in the respiration calorimeter prove that patients as a result of the fasting acquire the power of oxidizing sugar derived first from their own body protein and later from the protein and carbohydrate of a carefully regulated diet.

5. The respiratory quotients during fasting and after the glycosuria had ceased were in some such instances higher than can be easily explained by the oxidation of the materials supposedly available. Also the ingestion of alcohol was sometimes followed by respiratory quotients higher than would theoretically be expected. The data will be analyzed in a subsequent paper.

6. The specific dynamic action of food, especially fat, was apparently normal in a patient with moderately severe diabetes.

7. The results of two respiration experiments in a severely diabetic patient have shown that mild exercise slightly raises the quotient, and this suggests the possibility that exercise may improve carbohydrate utilization. Generalizations or positive conclusions from these experiments are not attempted.

8. According to comparisons of the surface area as calculated by the linear formula, increase of the basal metabolism above the true normal level in severe diabetes is generally absent or slight. The metabolism was shown to fall markedly during fasting, to 20 per cent. below normal. The level of metabolism in diabetes is the resultant of a number of forces; for example, increased destruction of protein and perhaps other processes tending to increase metabolism, and undernutrition, muscular relaxation (as in prolonged confinement in bed) and other possible conditions tending to diminish metabolism. According as one or the other of these groups of forces predominate, a higher or lower metabolism may be expected in any individual case of diabetes.